

#4

FIG. 1A

1 agggagagggc agtgaccatg aaggctgtgc tgcttgccct gttgatggca
51 ggcttgggccc tgcagccagg cactgccctg ctgtgctact cctgcaaagc
101 ccaggtgagc aacgaggact gcctgcaggt ggagaactgc acccagctgg
151 gggagcagtg ctggaccgcg cgcctccgcg cagttggcct cctgaccgtc
201 atcagcaaag gctgcagctt gaactgctg gatgactcac aggactacta
251 cgtgggcaag aagaacatca cgtgctgtga caccgacttg tgcaacgcca
301 gcgggggccca tgccctgcag ccggctgccg ccctccttgc gctgctccct
351 gcactcggcc tgctgctctg gggaccgccc cagctatagg ctctgggggg
401 ccccgctgca gccacactg ggtgtggtgc ccaggcctt tgtgccactc
451 ctcacagaac ctggcccagt gggagcctgt cctggttcct gaggcacatc
501 ctaacgcaag tttgaccatg tatgtttgca ccccttttcc ccnaaccctg
551 accttcccat gggccttttc caggattccn accnggcaga tcagttttag
601 tganacanat ccgcntgcag atggcccctc caaccntttn tgttgntggt
651 tccatggccc agcatttttc acccttaacc ctgtgttcag gcacttnttc
701 ccccaggaag ccttccctgc ccacccatt tatgaattga gccaggtttg
751 gtccgtggtg tccccgcac ccagcagggg acaggcaatc aggagggccc
801 agtaaaggct gagatgaagt ggactgagta gaactggagg acaagagttg
851 acgtgagttc ctgggagttt ccagagatgg ggcctggagg cctggaggaa
901 ggggccaggc ctcacatttg tgggntccc gaatggcagc ctgagcacag
951 cgtaggccct taataaacac ctgttgata agccaaaaaa aaaaaaa

FIG. 1B

MKAVLLALLMAGLALQPGTALLCYSCKAQVSNECLQV
ENCTQLGEQCWTARIRAVGLLTVISKGCSLNCVDDS
QDYVVGKKNITCCDLDLCNASGAHALQPAAAILALLPAL
GLLLWGPGQL

FIG. 2

1 ATGAAGACAGTTTTTTTTATCCTGCTGGCCACCTACTTAGCCCTGCATCCAGGTGCTGCT
 -----+-----+-----+-----+-----+-----+ 60
 TACTTCTGTCAAAAAAAAAATAGGACGACCGGTGGATGAATCGGGACGTAGGTCCACGACGA

 M K T V F F I L L A T Y L A L H P G A A

 61 CTGCAGTGCTATTCATGCACAGCACAGATGAACAACAGAGACTGTCTGAATGTACAGAAC
 -----+-----+-----+-----+-----+-----+ 120
 GACGTACAGATAAGTACGTGTCGTGTCTACTTGTGTCTCTGACAGACTTACATGTCTTG

 L Q C Y S C T A Q M N N R D C L N V Q N

 121 TGCAGCCTGGACCAGCACAGTTGCTTTACATCGCGCATCCGGGCCATTGGACTCGTGACA
 -----+-----+-----+-----+-----+-----+ 180
 ACGTCGGAECTGGTCGTGTCAACGAAATGTAGCGCGTAGGCCCGGTAACCTGAGCACTGT

 C S L D Q H S C F T S R I R A I G L V T

 181 GTTATCAGTAAGGGCTGCAGCTCACAGTGTGAGGATGACTCGGAGAACTACTATTTGGGC
 -----+-----+-----+-----+-----+-----+ 240
 CAATAGTCATTCCCGACGTCGAGTGTCACTCCTACTGAGCCTCTTGATGATAAACCCG

 V I S K G C S S Q C E D D S E N Y Y L G

 241 AAGAAGAACATCACGTGCTGCTACTCTGACCTGTGCAATGTCAACGGGGCCACACCCTG
 -----+-----+-----+-----+-----+-----+ 300
 TTCTTCTGTAGTGCACGACGATGAGACTGGACACGTTACAGTTGCCCCGGGTGTGGGAC

 K K N I T C C Y S D L C N V N G A H T L

 301 AAGCCACCCACCACCCTGGGGCTGCTGACCGTGCTCTGCAGCCTGTTGCTGTGGGGCTCC
 -----+-----+-----+-----+-----+-----+ 360
 TTCGGTGGGTGGTGGGACCCGACGACTGGCACGAGACGTCGGACAACGACACCCCGAGG

 K P P T T L G L L T V L C S L L L W G S

 361 AGCCGTCTGTAGGCTCTGGGAGAGCCTACCATAGCCCGATTGTGAAGGGATGAGCTGCAC
 -----+-----+-----+-----+-----+-----+ 420
 TCGGCAGACATCCGAGACCCTCTCGGATGGTATCGGGCTAACACTTCCCTACTCGACGTG

 S R L *

 421 TCCACCCACCCCCACACAGG
 -----+-----+ 441
 AGGTGGGGTGGGGGTGTGTCC

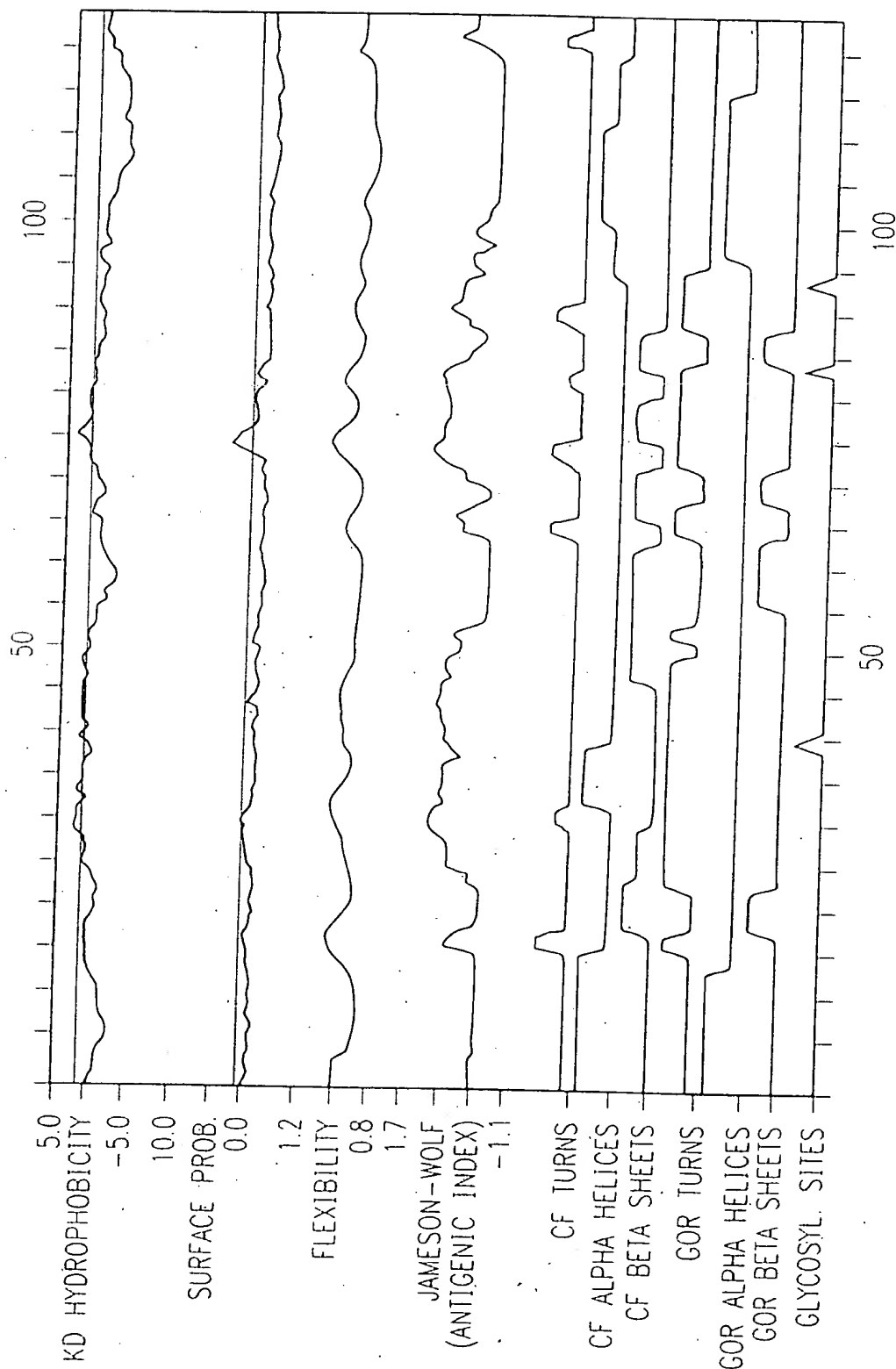
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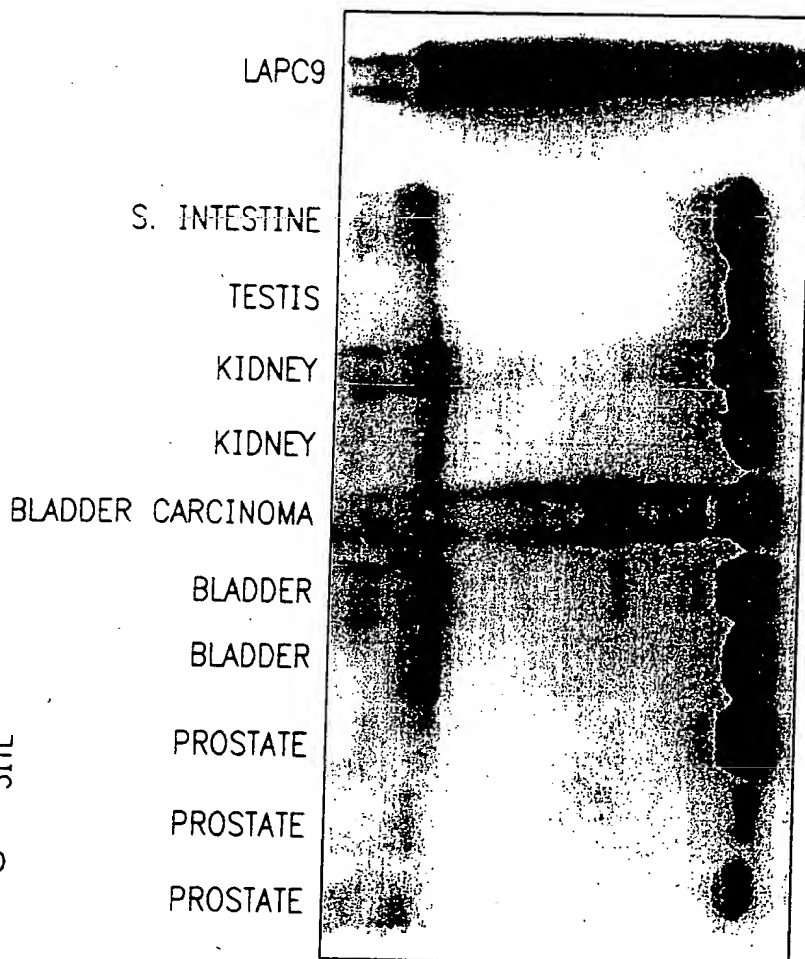
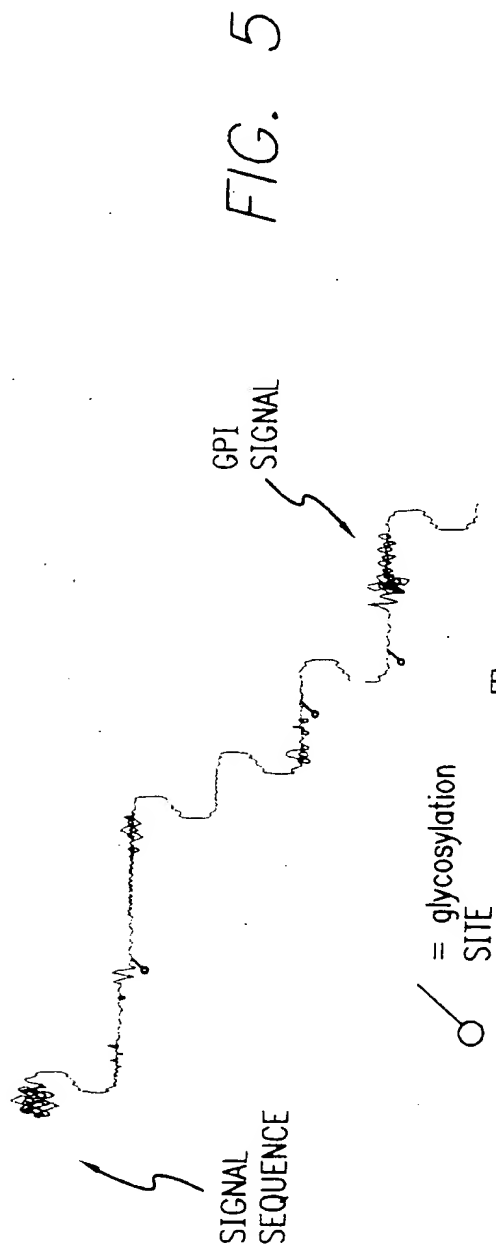
FIG. 3

1	M	K	I	F	L	P	V	L	L	A	A	L	L	G	V	E	R	A	S	S		hSCA-2
1	M	K	A	V	L	L	A	L	L	M	A	G	L	A	L	Q	P	G	T	A		hPSCA
1	M	K	T	V	L	F	L	L	A	T	Y	L	A	L	H	P	G	A	A			mPSCA
21	L	M	C	F	S	C	L	N	Q	K	S	N*	L	Y	C	L	K	P	T	I		
21	L	L	C	Y	S	C	K	A	Q	V	S	N*	E	D	C	L	Q	V	E	N*		
21	L	Q	C	Y	S	C	T	A	Q	M	N	N*	R	D	C	L	N	V	Q	N*		
41	C	S	D	Q	D	N	Y	C	V	T	V	S	A	S	A	G	I	G	N	L		
41	C	T	Q	L	G	E	Q	C	W	T	A	R	I	R	A	V	G	L	L	T		
41	C	S	L	D	Q	H	S	C	F	T	S	R	I	R	A	I	G	L	V	T		
61	V	T	F	G	H	S	L	S	K	T	C	S	P	A	C	P	I	P	E	G		
61	V	-	-	-	-	-	-	I	S	K	G	C	S	L	N	C	V	D	D	S	Q	
61	V	-	-	-	-	-	-	I	S	K	G	C	S	S	Q	C	E	D	D	S	E	
81	V	N	V	G	V	A	S	M	G	I	S	C	C	Q	S	F	L	C	N*	F		
76	D	Y	Y	V	G	K	K	-	N*	I	T	C	C	D	T	D	L	C	N*	A		
76	N	Y	Y	L	G	K	K	-	N*	I	T	C	C	Y	S	D	L	C	N*	V		
101	S	A	A	D	G	G	L	R	A	S	V	T	L	L	G	A	G	L	L	L		
95	S	G	A	H	A	L	O	P	A	A	A	I	L	A	L	L	P	A	L	G		
95	N	G	A	H	T	L	K	P	P	T	T	L	G	L	L	T	V	L	C	S		
121	S	L	L	P	A	L	L	R	F	G	P											
115	L	L	L	W	G	P	G	Q	L	-	-											
115	L	L	L	W	G	S	S	R	L	-	-											

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FIG. 4





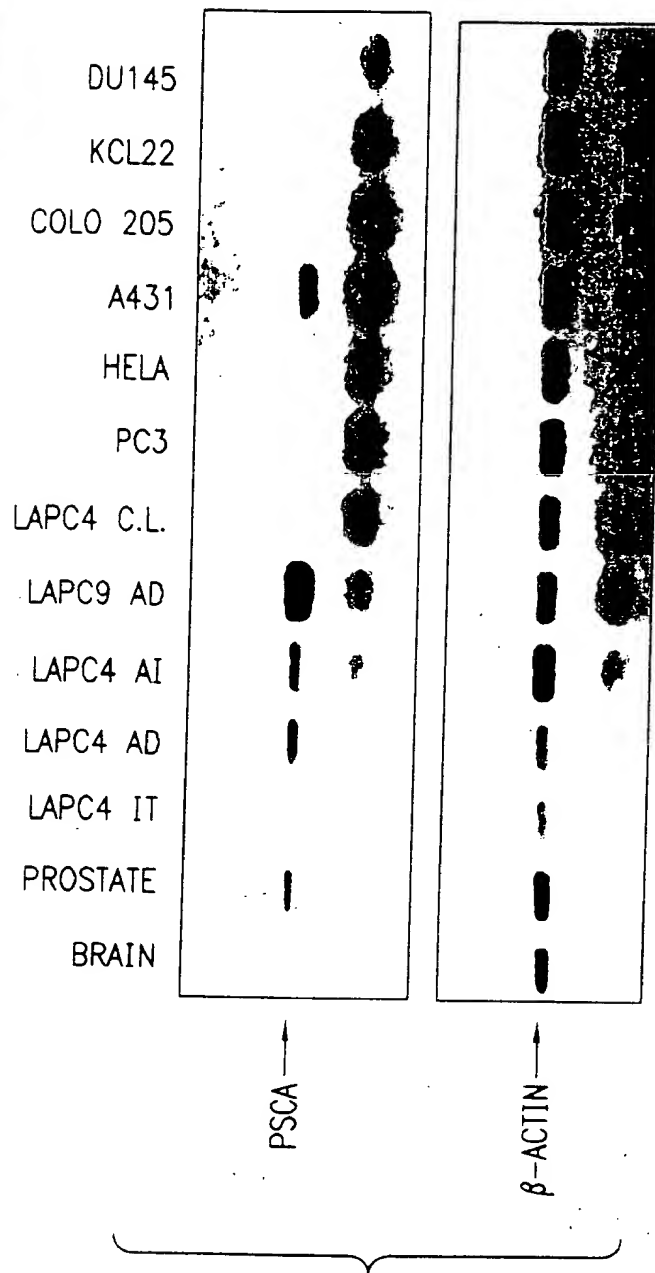
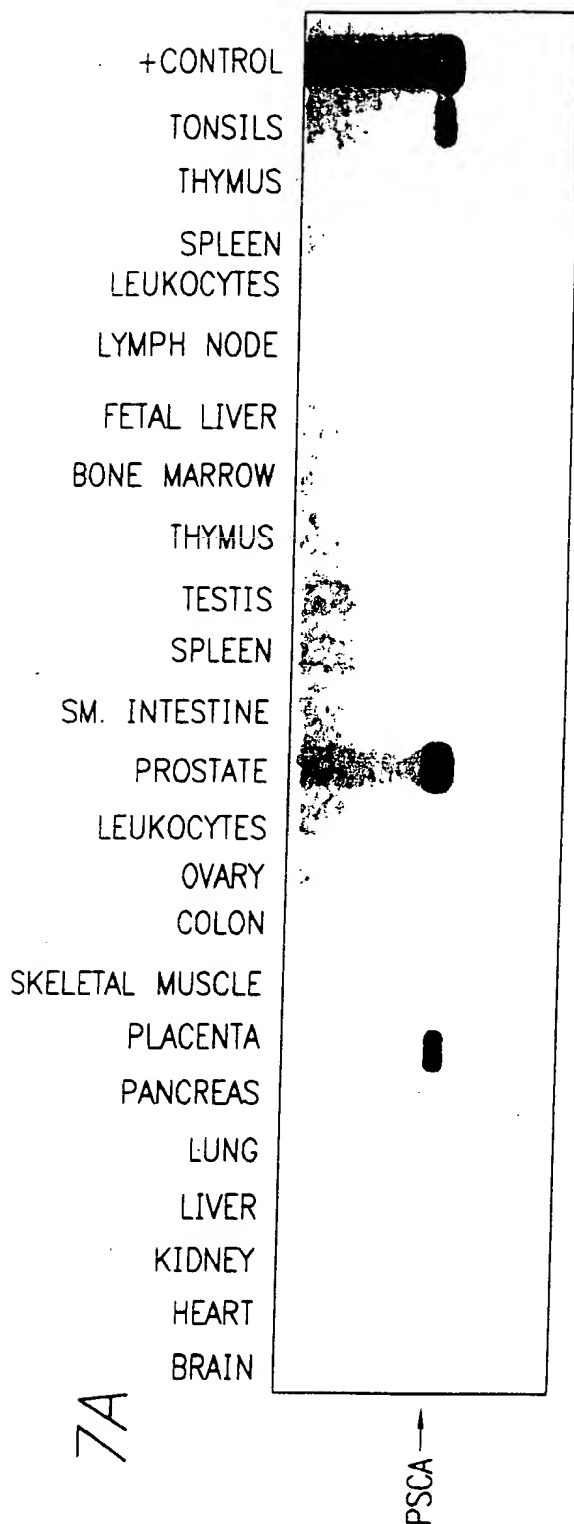


FIG. 8A

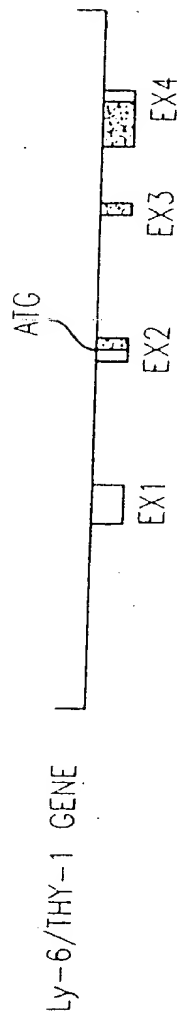


FIG. 8B

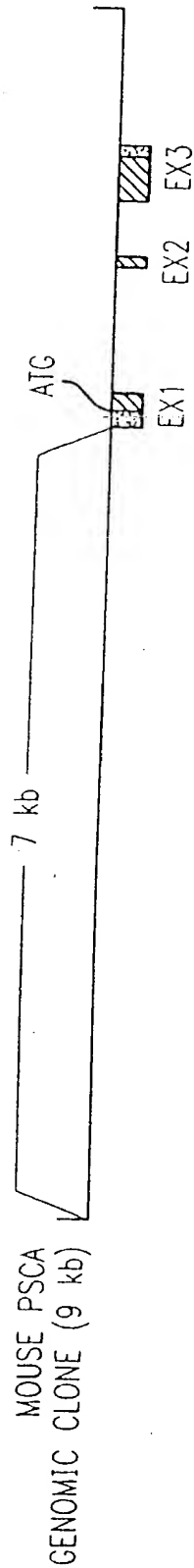
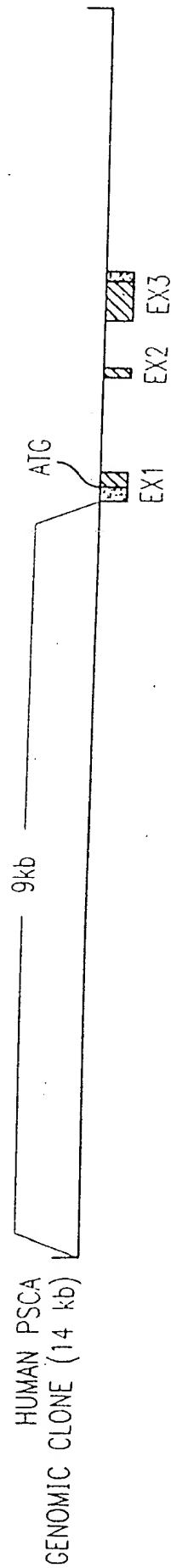


FIG. 8C



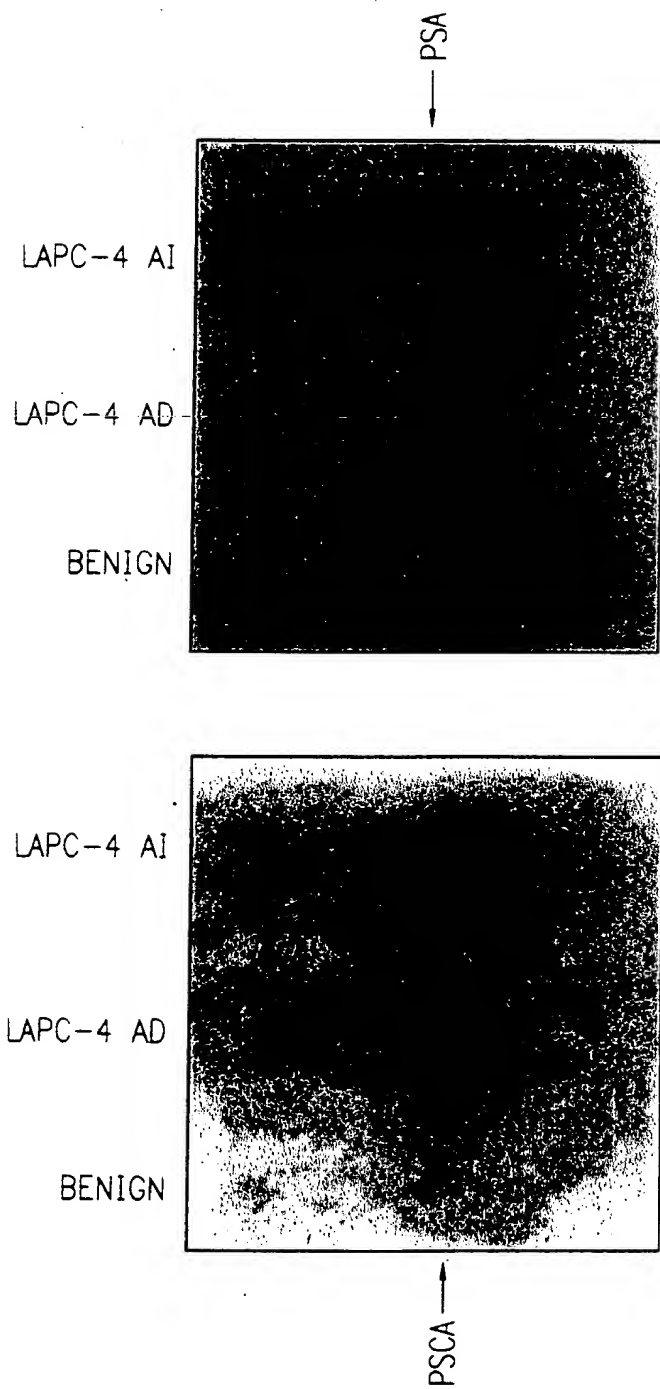


FIG. 9A

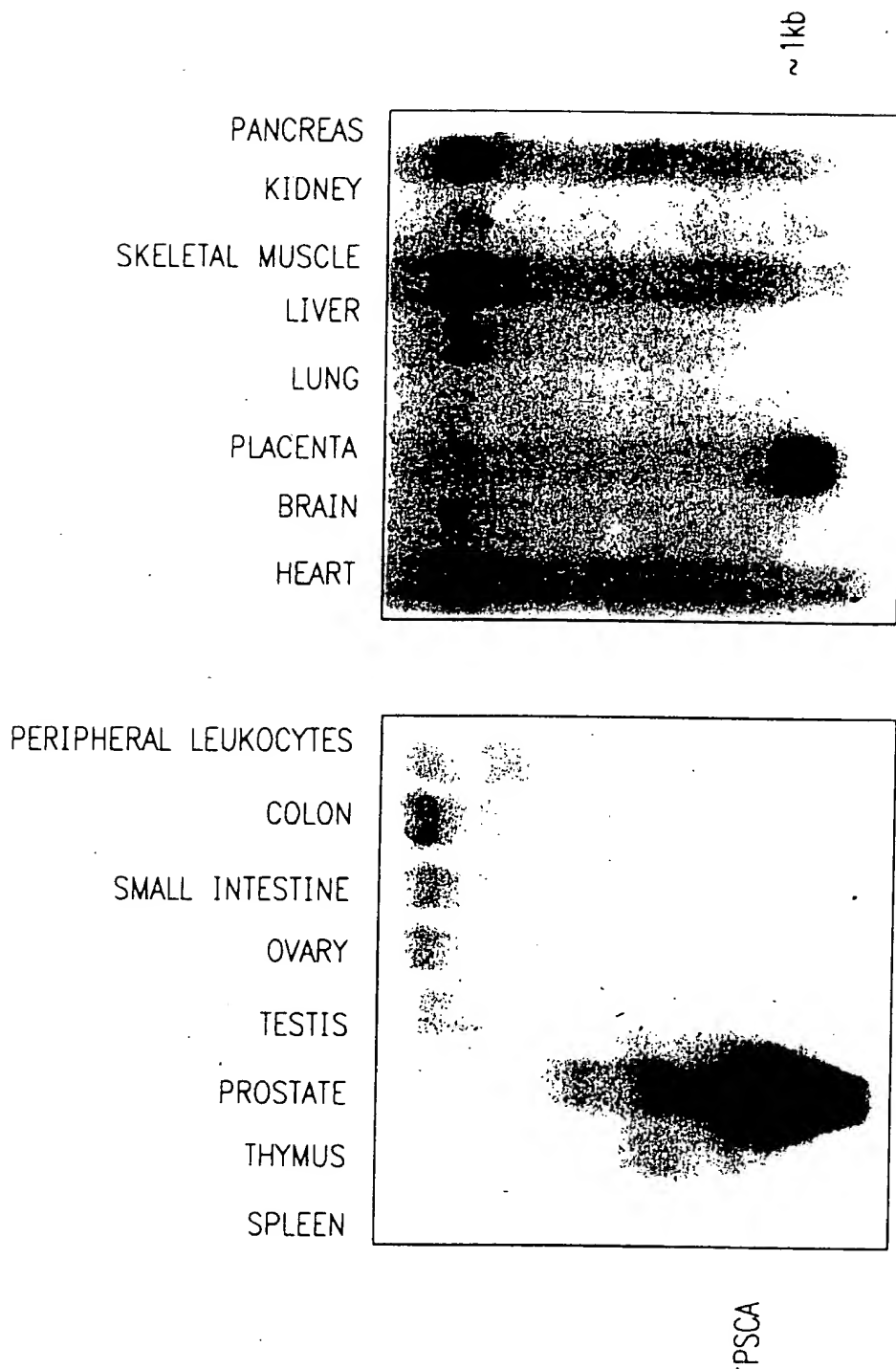


FIG. 9B

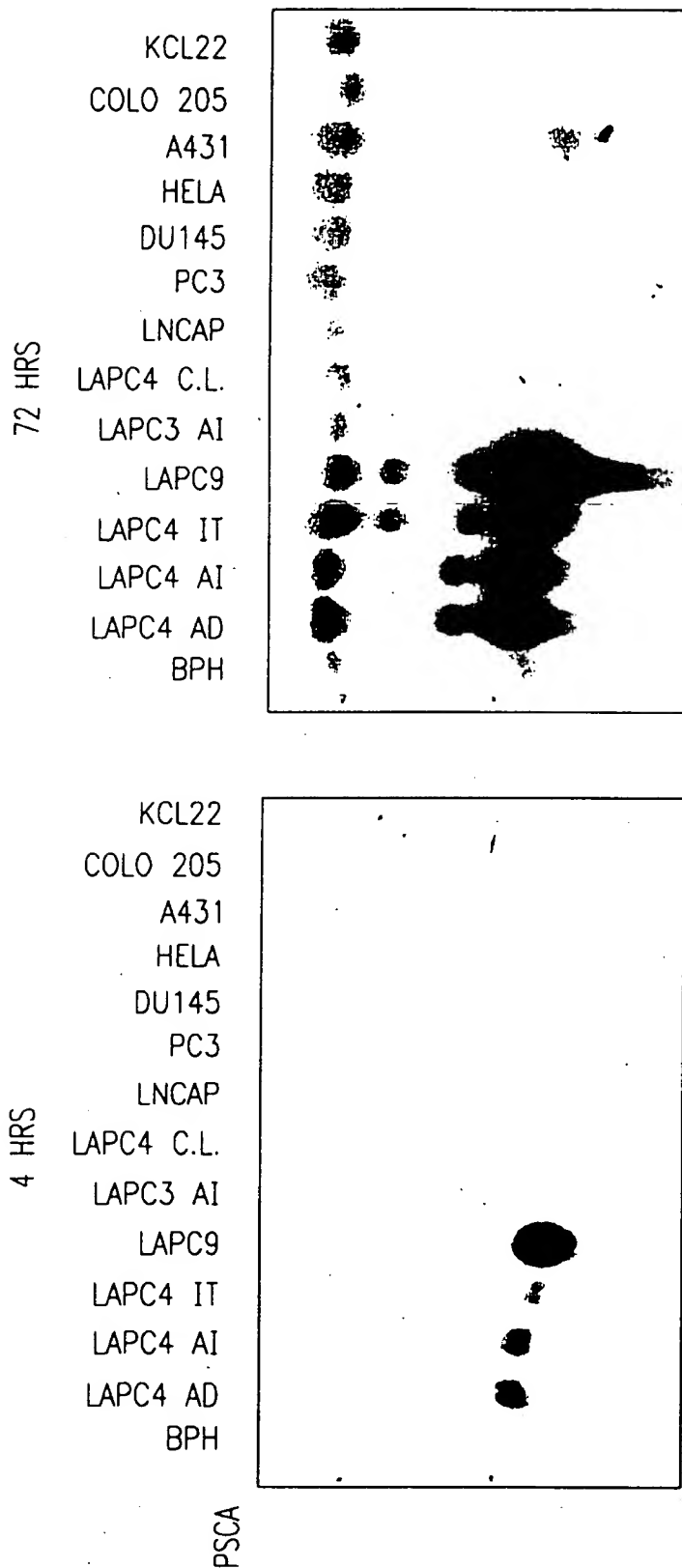


FIG. 10A

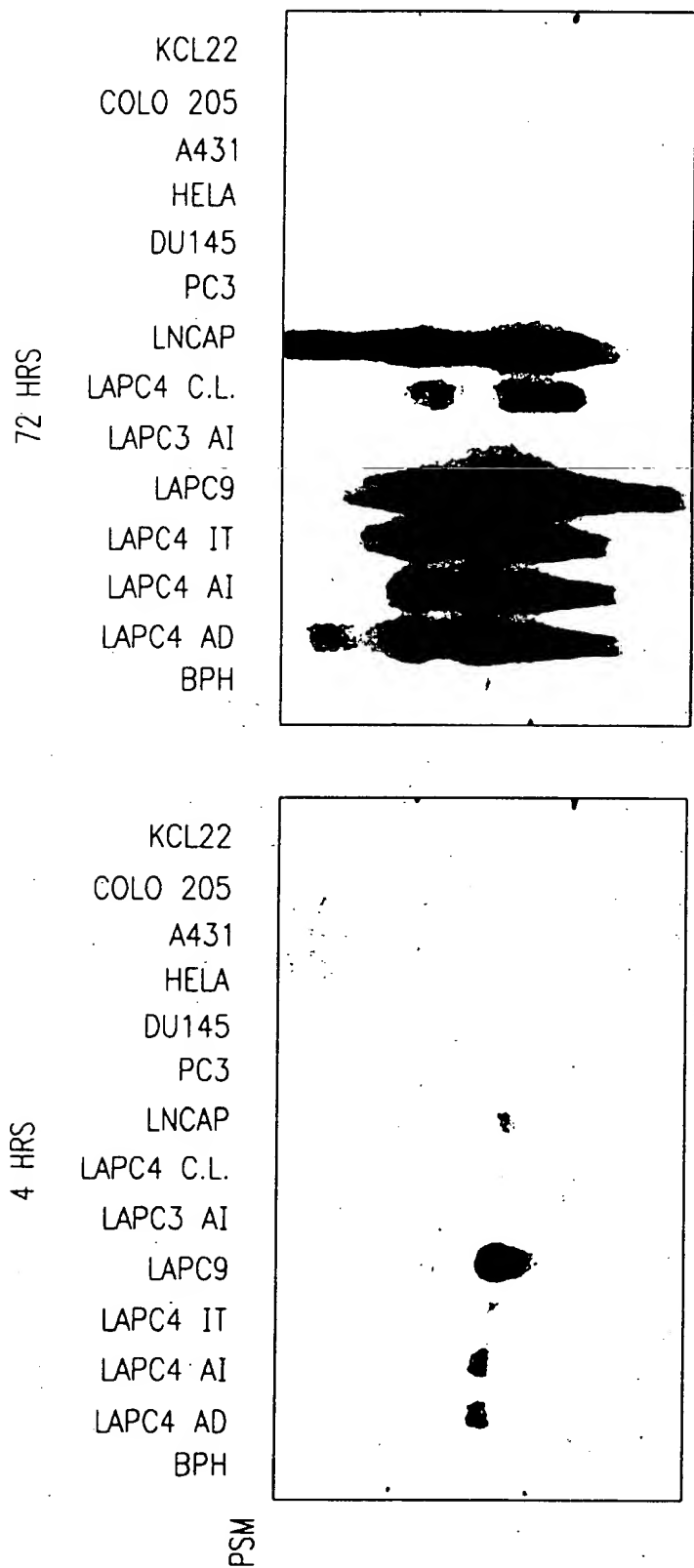


FIG. 10B

FO5240" TFB45860

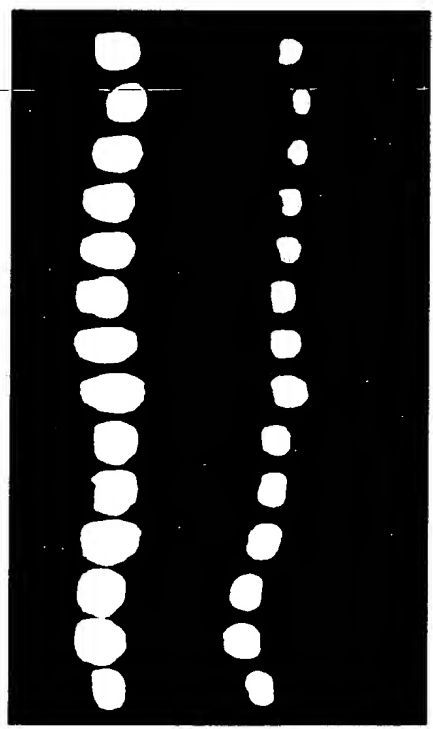
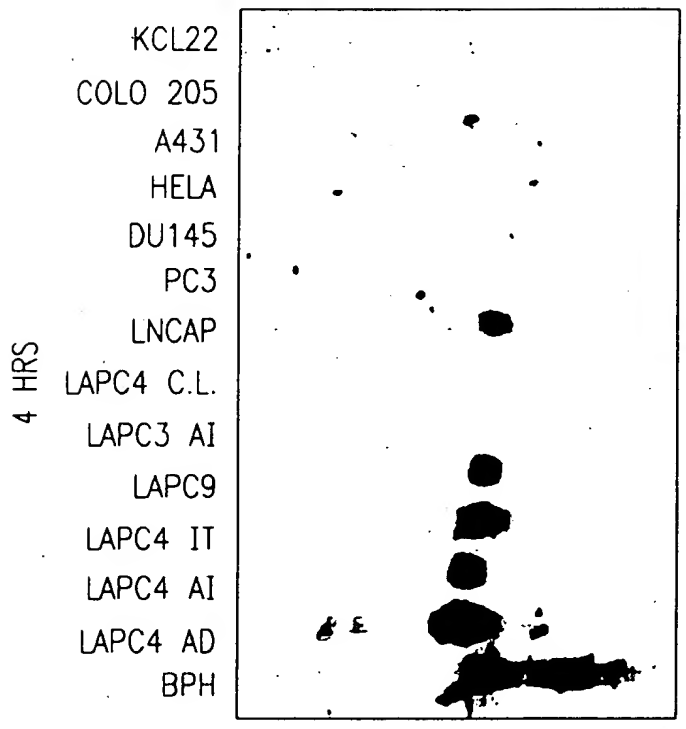
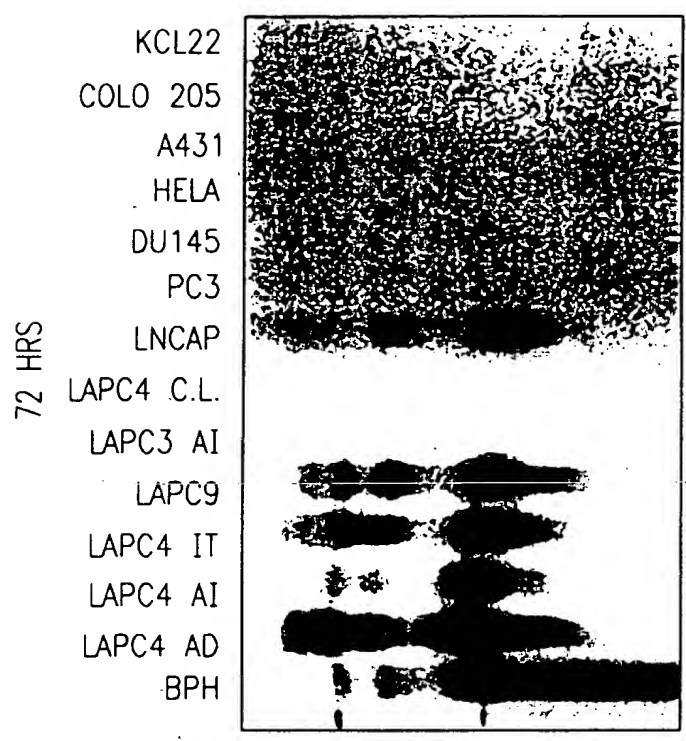


FIG. 10C

FIG. 11A



FIG. 11B

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FIG. 11C

O GLYCOSIDASE
N GLYCOSIDASE F
CONTROL

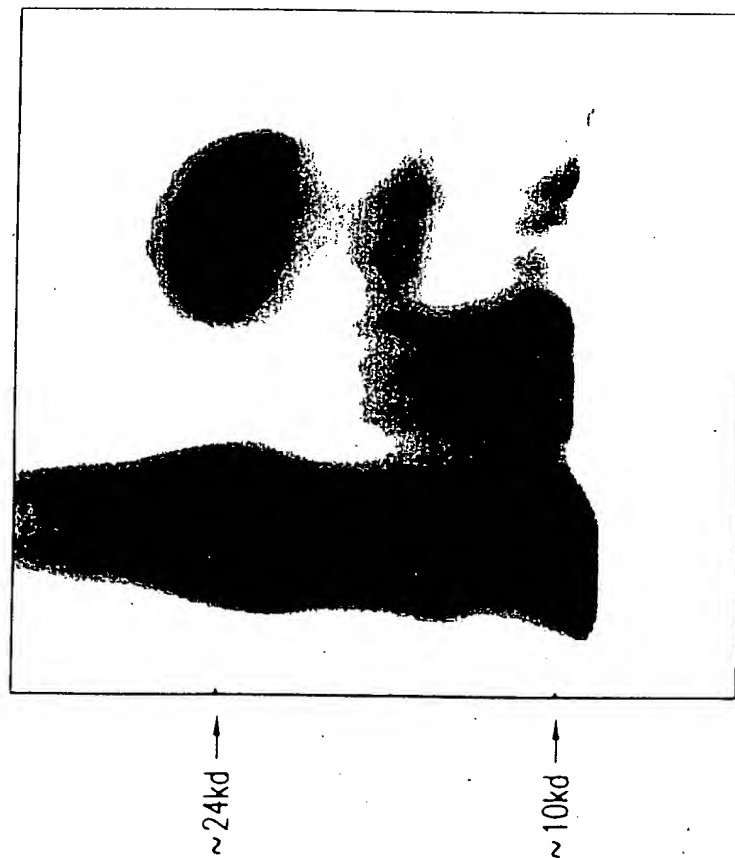


FIG. 12A

CELL ASSOCIATED
SECRETED

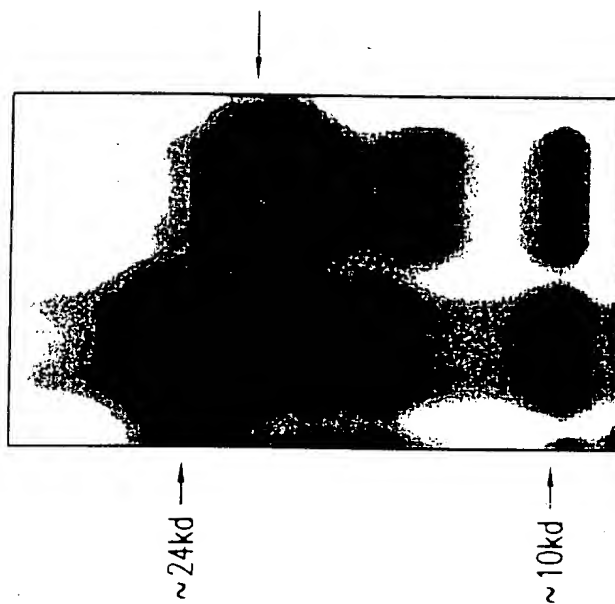


FIG. 12B

FO5220" FT845860

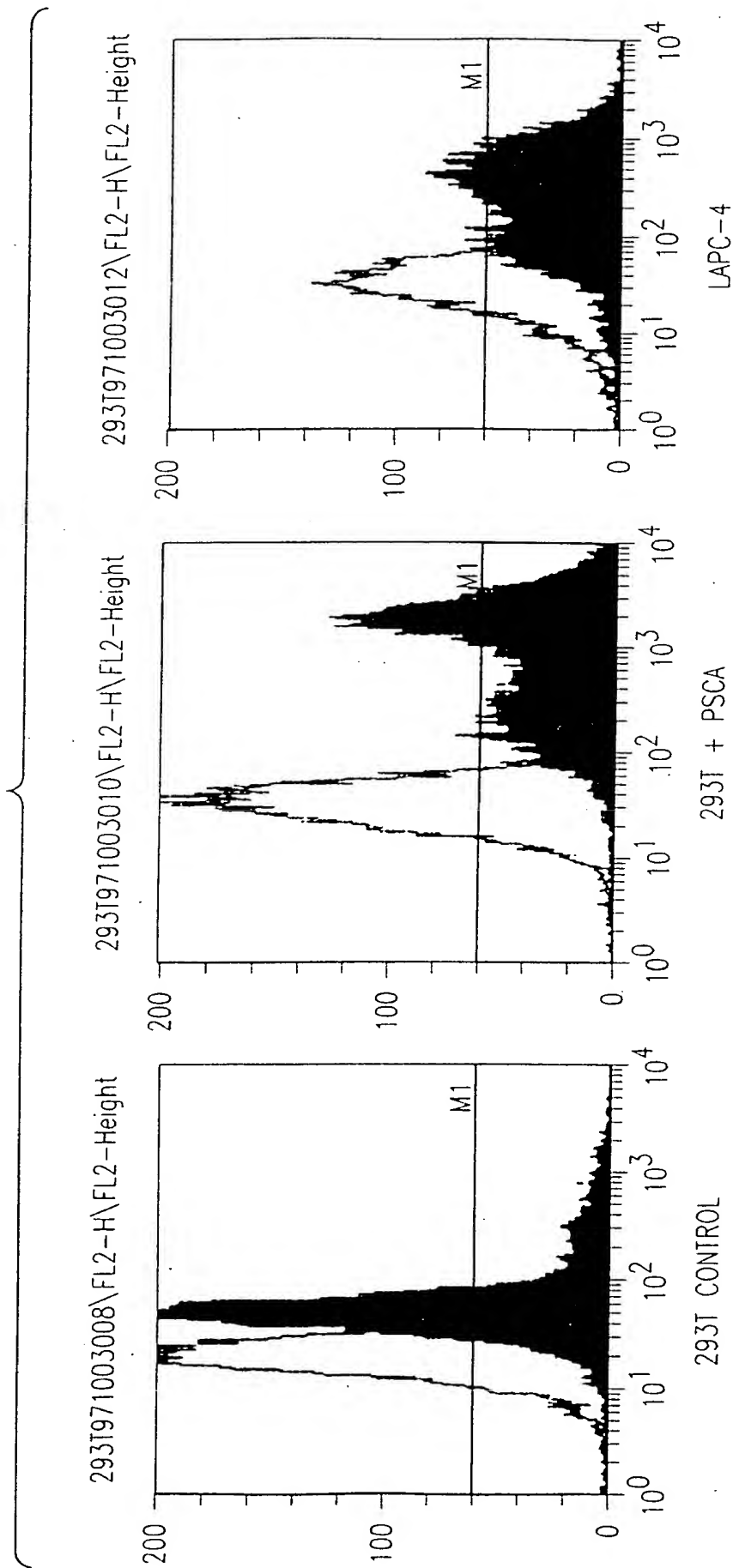


FIG. 12C

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FIG. 13

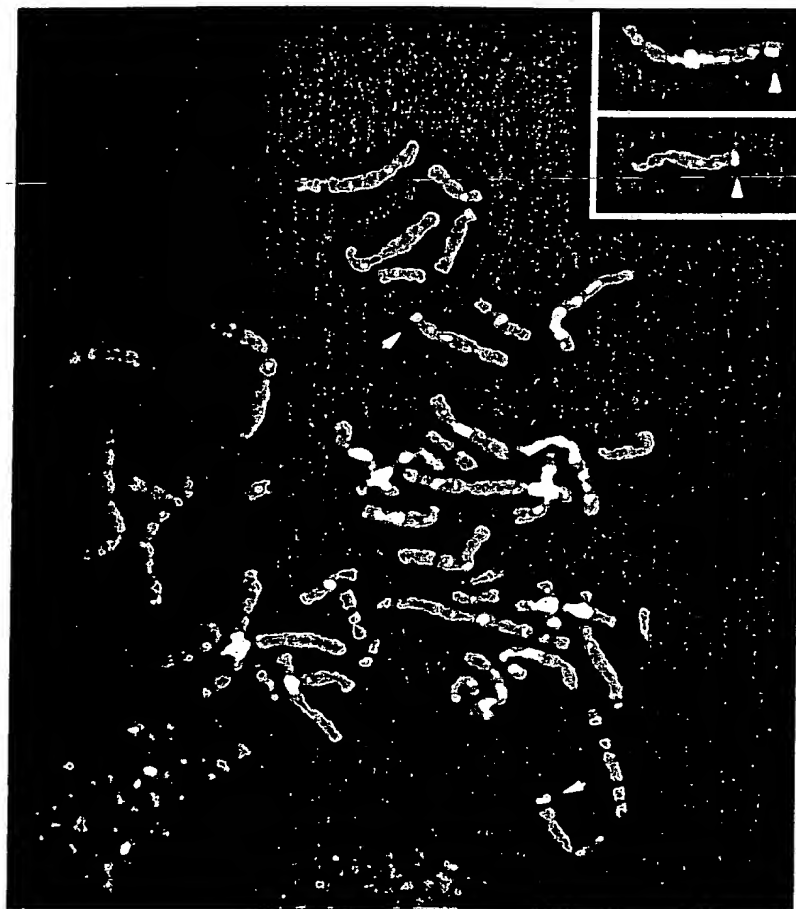


FIG. 14A

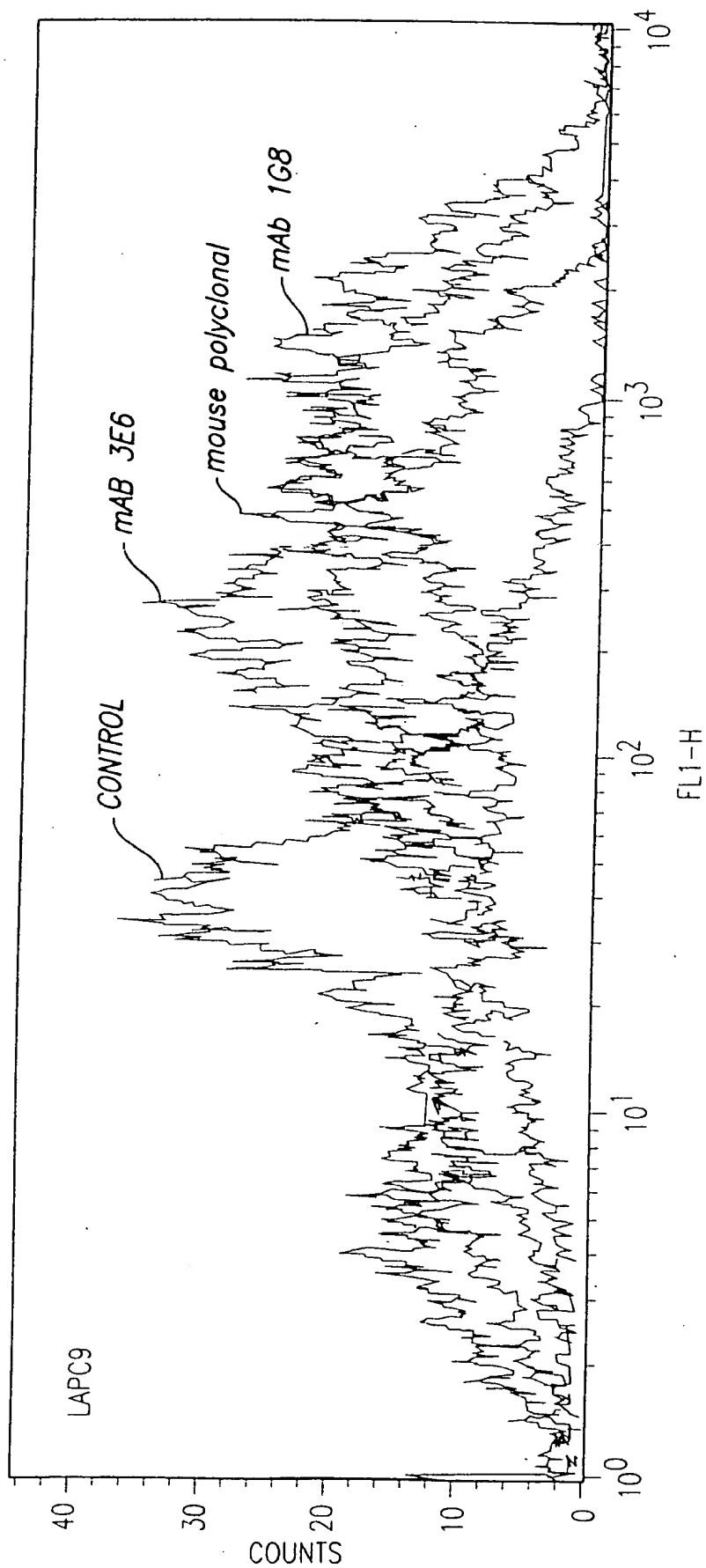


FIG. 14B

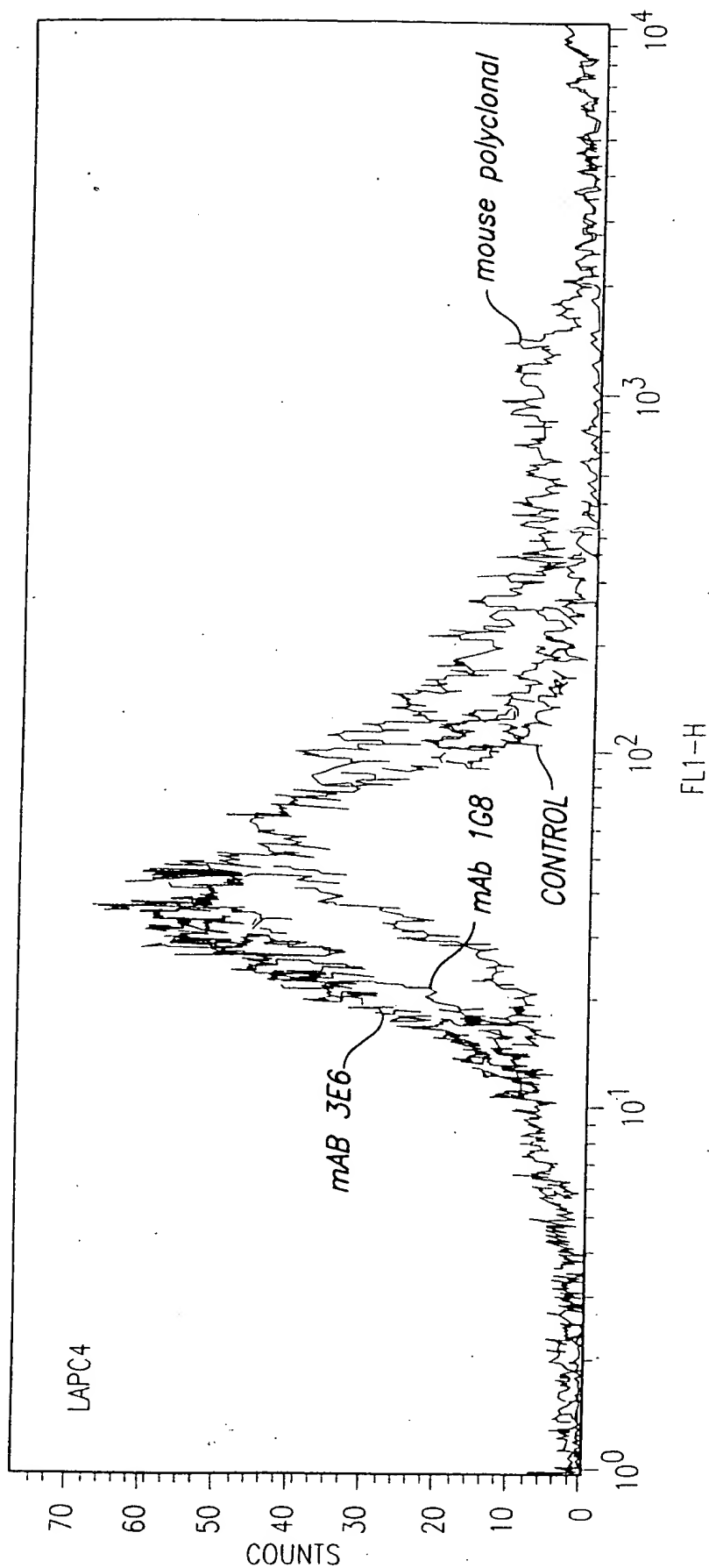
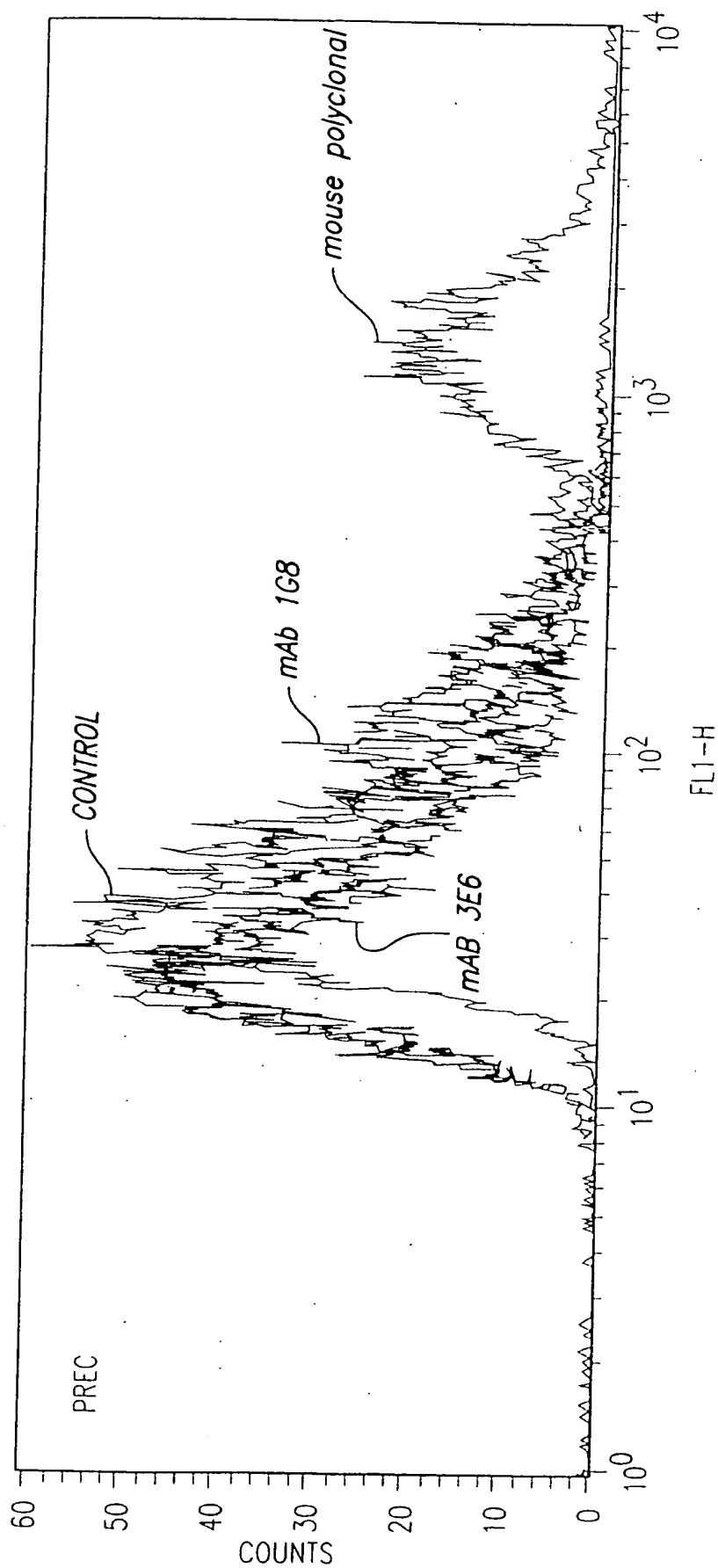


FIG. 14C



EPIIOPPE MAP

mAb	ISOTYPE	FL (18-98)	N (2-50)	M (46-109)	C (85-123)
1G8	IgG1 k	2.039	0.007	0.628	0.000
2H9	IgG1 k	1.318	0.863	0.032	0.021
3C5	IgG2a k	2.893	1.965	0.016	0.005
3E6	IgG3 k	0.328	0.024	0.069	0.370
4A10	IgG2a k	2.039	1.315	0.000	0.014
2A2	IgG2a k	1.366	0.733	0.010	0.003
3G3	IgG2a k	2.805	1.731	0.004	0.000

FIG. 15A

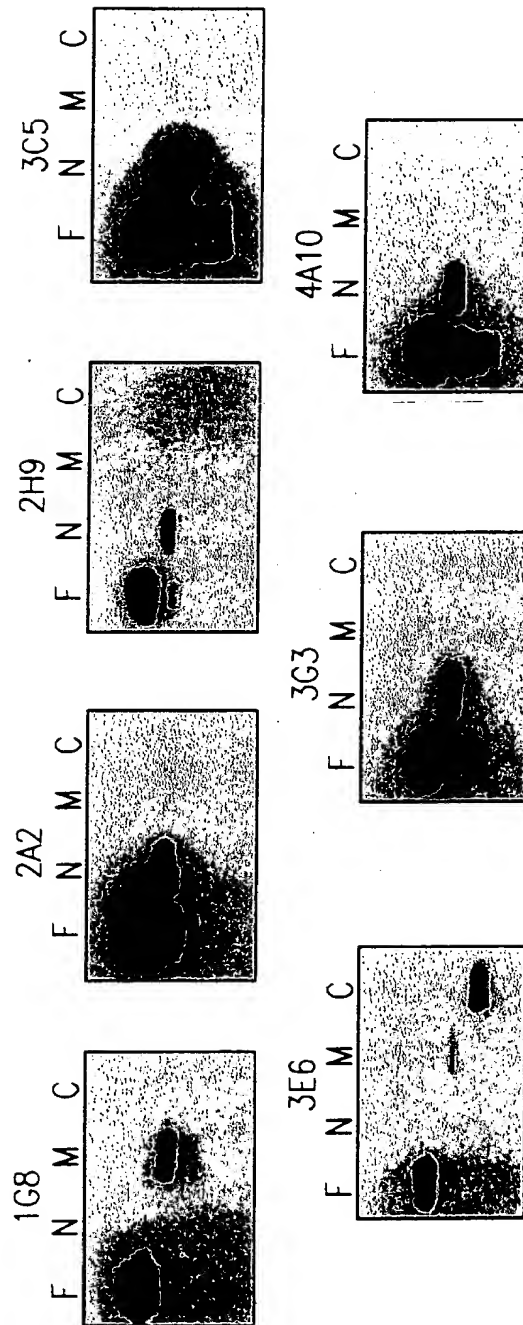


FIG. 15B

PROSTATE STEM CELL ANTIGEN (PSCA) IS A GPI-ANCHORED PROTEIN

1	M	K	I	F	P	V	L	A	A	L	L	G	V	E	R	A	S	S	hSCA-2
1	M	K	A	V	L	L	A	L	M	A	G	L	A	L	Q	P	C	T	hPSCA
1	M	K	T	V	L	F	L	L	A	T	Y	L	A	L	H	P	C	A	mPSCA
21	L	M	C	F	S	C	L	N	Q	K	S	N	L	Y	C	L	K	P	T
21	L	L	C	Y	S	C	K	A	Q	V	S	N	E	D	C	L	Q	V	E
21	L	Q	C	Y	S	C	T	A	Q	M	N	N	R	D	C	L	N	V	Q
41	C	S	D	Q	D	N	Y	C	V	T	V	S	A	S	A	G	I	G	N
41	C	T	Q	L	G	E	Q	C	W	T	A	P	P	A	V	G	L	L	T
41	C	S	L	D	Q	H	S	C	F	I	S	R	R	A	I	G	L	V	T
61	V	T	F	G	H	S	L	S	K	T	C	S	P	A	C	P	I	P	E
61	V	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
61	V	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
81	V	N	V	G	V	A	S	M	G	T	S	C	C	Q	Q	S	F	L	C
76	D	Y	Y	V	G	K	K	-	-	-	-	-	-	-	-	-	-	-	-
76	N	Y	Y	L	G	K	K	-	-	-	-	-	-	-	-	-	-	-	-
101	S	A	A	D	G	G	L	R	A	S	V	T	T	L	G	A	G	L	L
95	S	C	A	H	A	L	Q	P	A	A	A	I	L	A	L	P	A	L	G
95	N	C	A	H	T	L	K	P	T	T	L	G	L	L	T	V	L	C	S
121	S	L	L	P	A	L	L	R	F	G	P	-	-	-	-	-	-	-	-
115	L	L	L	W	G	P	G	Q	-	-	-	-	-	-	-	-	-	-	-
115	L	L	L	W	G	S	S	R	-	-	-	-	-	-	-	-	-	-	-

FIG. 16A

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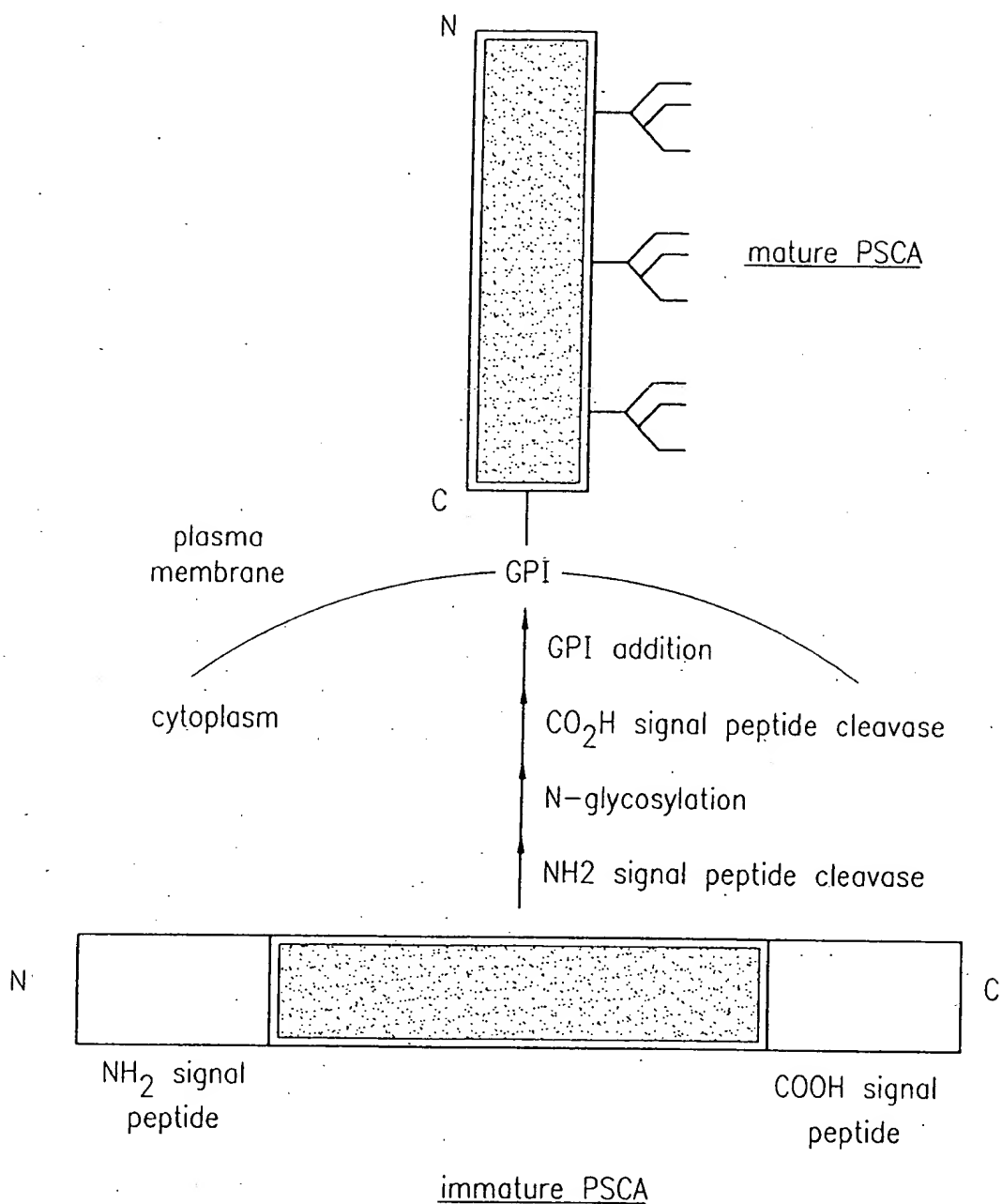
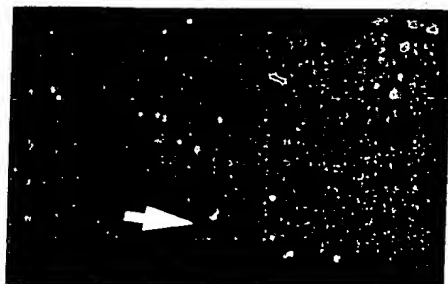


FIG. 16B

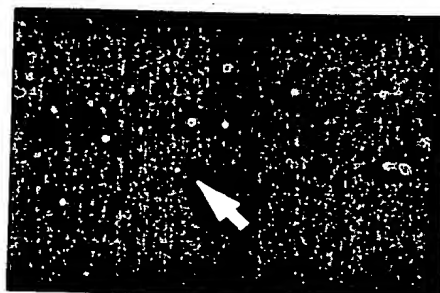
FIG. 17

GAIN CHROMOSOME 8



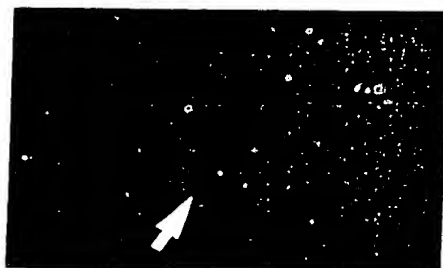
#34 c-myc

AMPLIFICATION



#75 c-myc

#34 PSCA



#75 PSCA

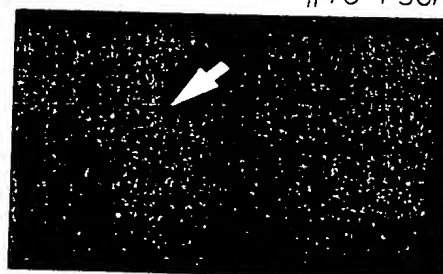
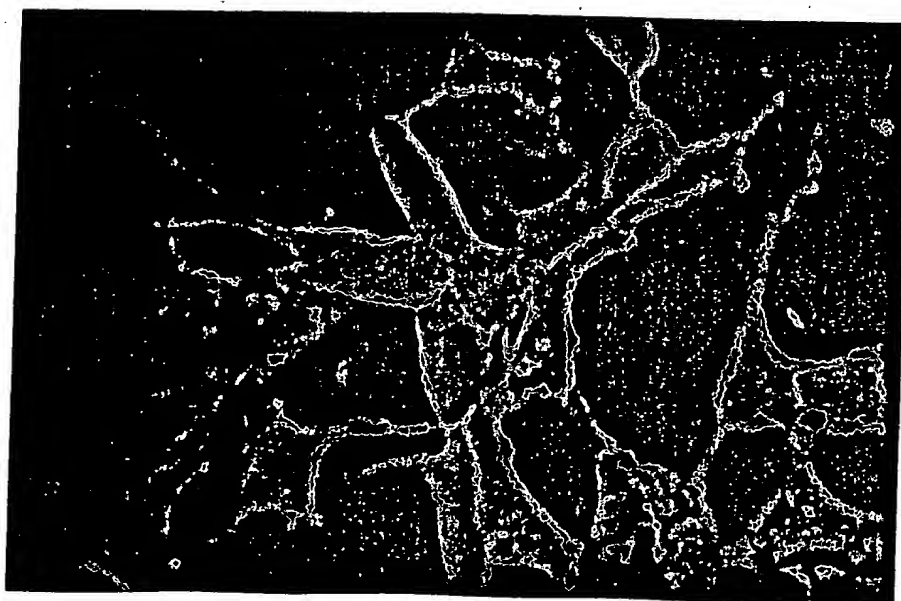


FIG. 18



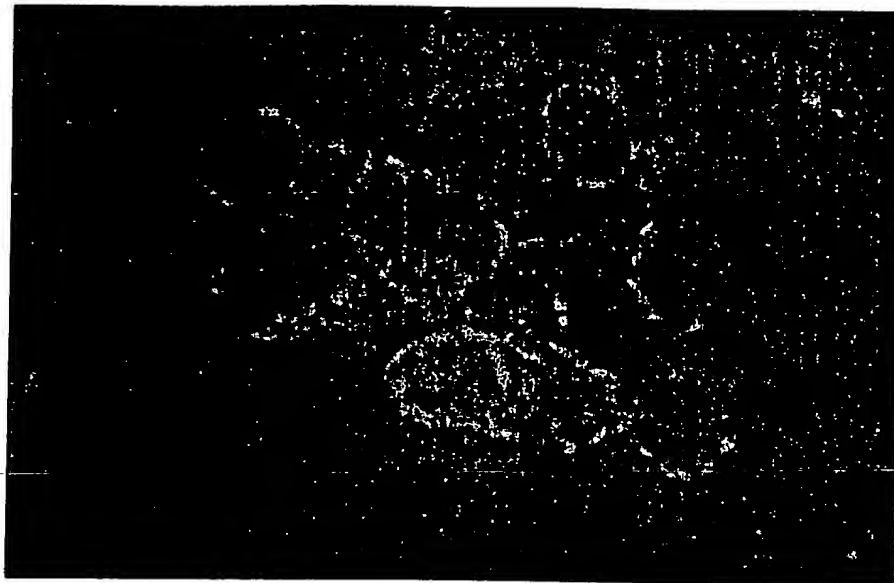


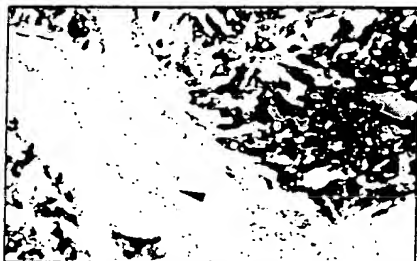
FIG. 19

FIG. 20

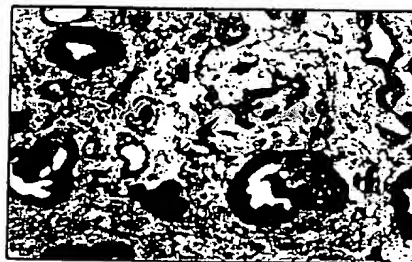


FIG. 21

PSCA IMMUNOSTAINING OF PRIMARY TUMORS



patient 1:mAb 1G8



patient 2:mAb 1G8



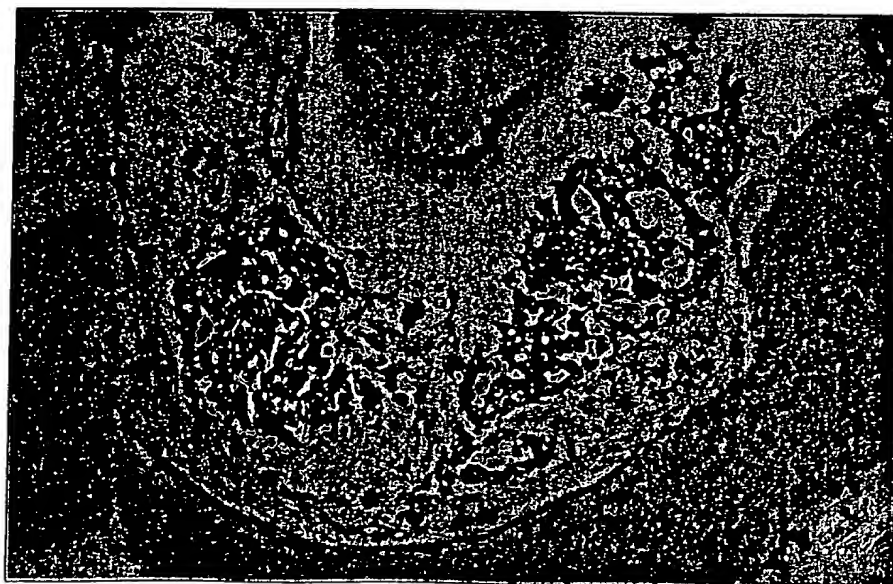
patient 3:mAb 1G8



patient 4:mAb 3E6



FIG. 22



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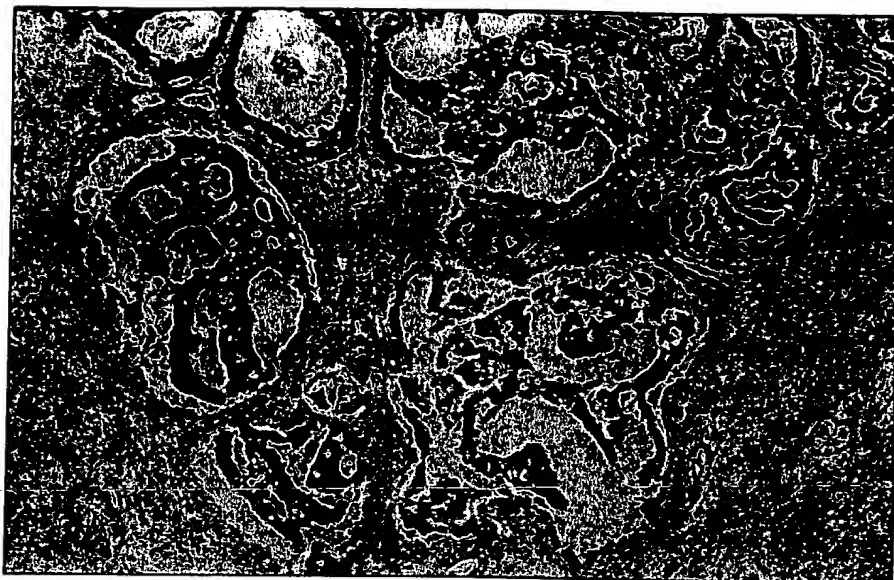


FIG. 23

FIG. 24



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FIG. 25

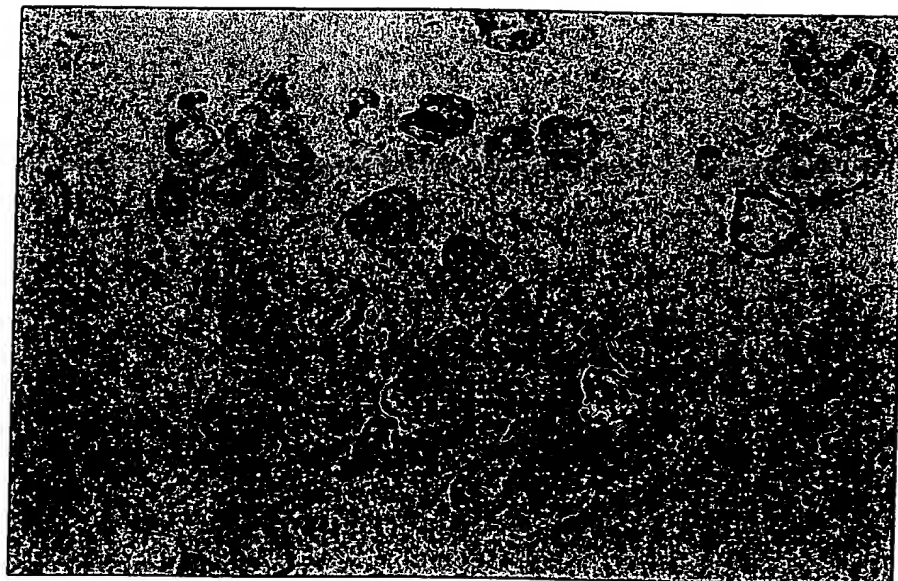
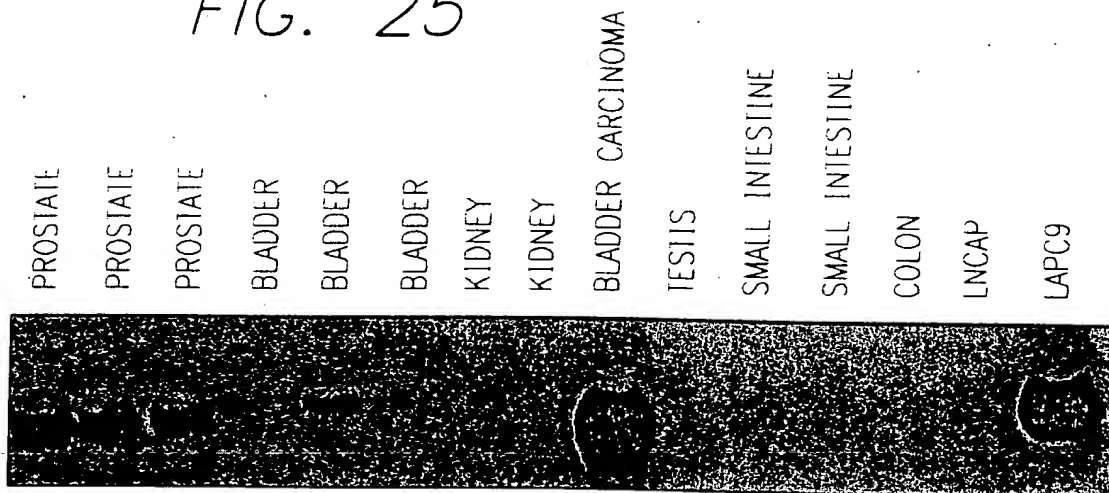


FIG. 26

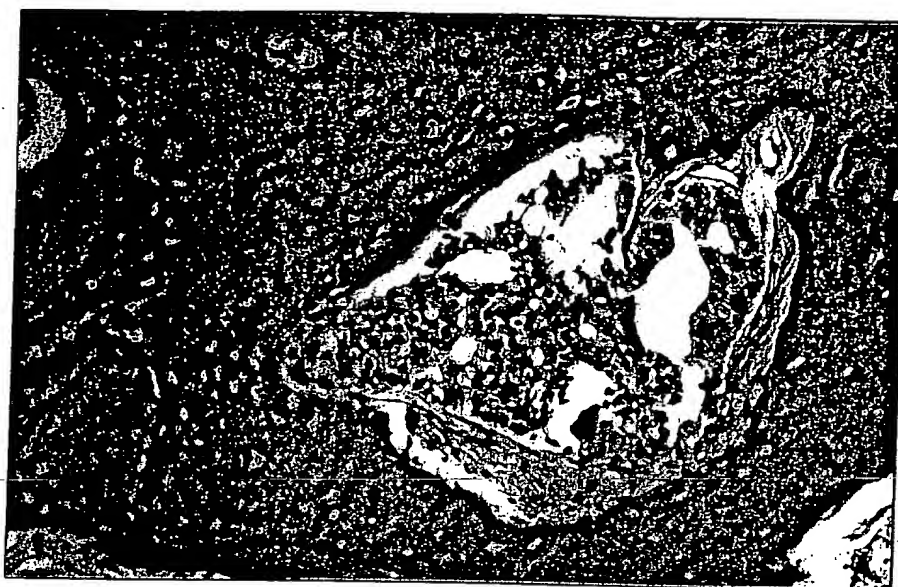
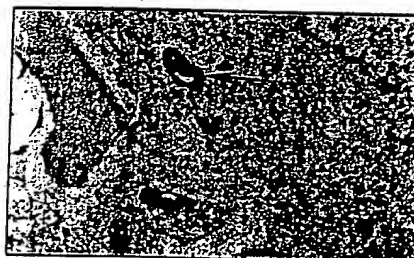
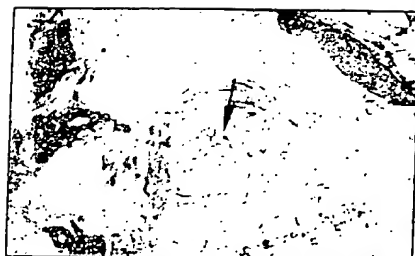
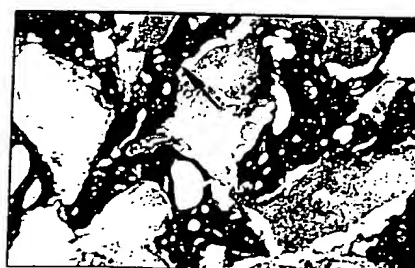


FIG. 27



Patient 5: H and E
and mAb 1G8



Patient 4: H and E
and mAb 3E6

FIG. 28

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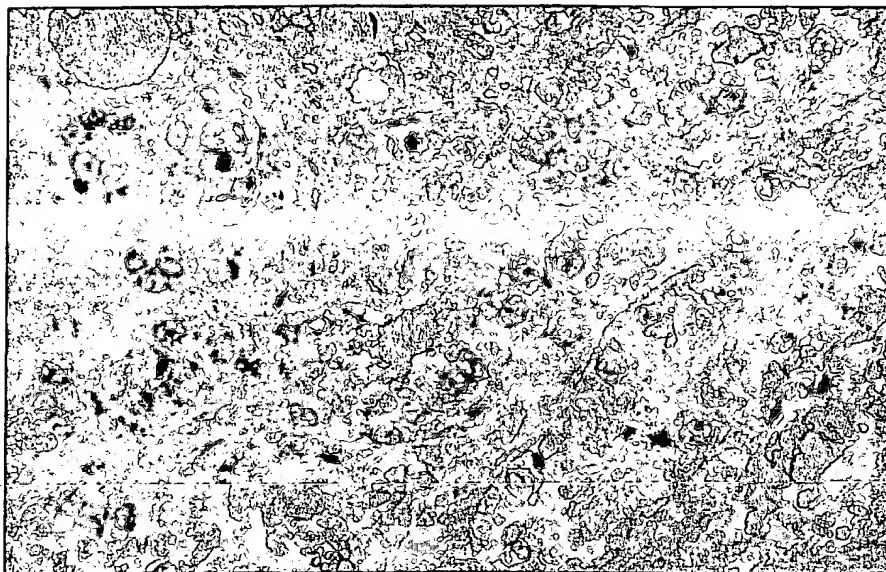
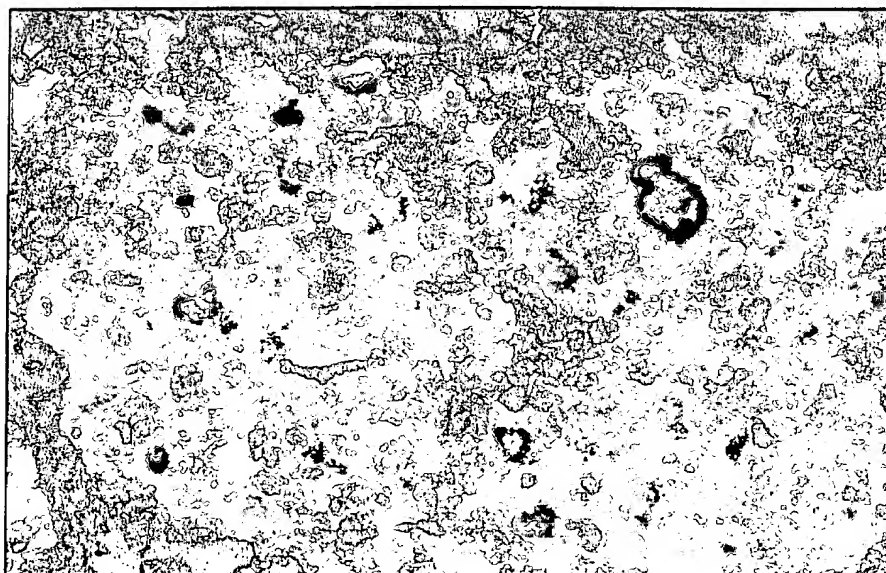


FIG. 29

FIG. 30



09854811.072501

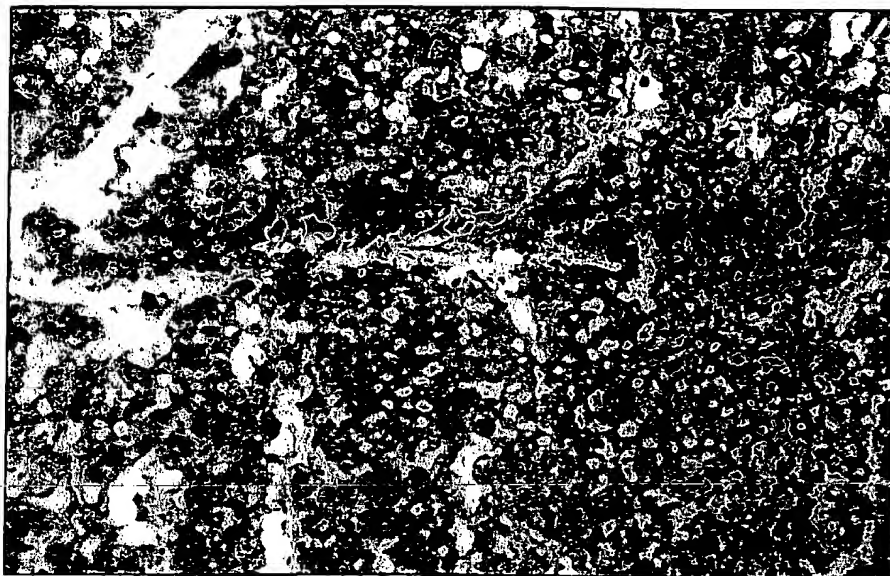


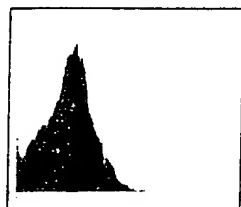
FIG. 31

FIG. 32

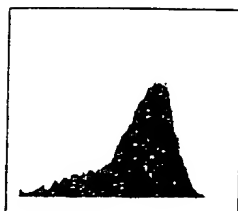


FIG. 33

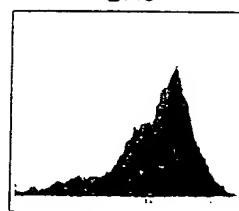
SECONDARY ANTIBODY



1G8



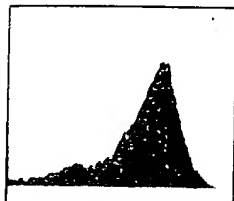
2H9



4A10



3C5



3E6

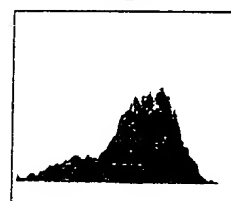


FIG. 34

FIG. 35

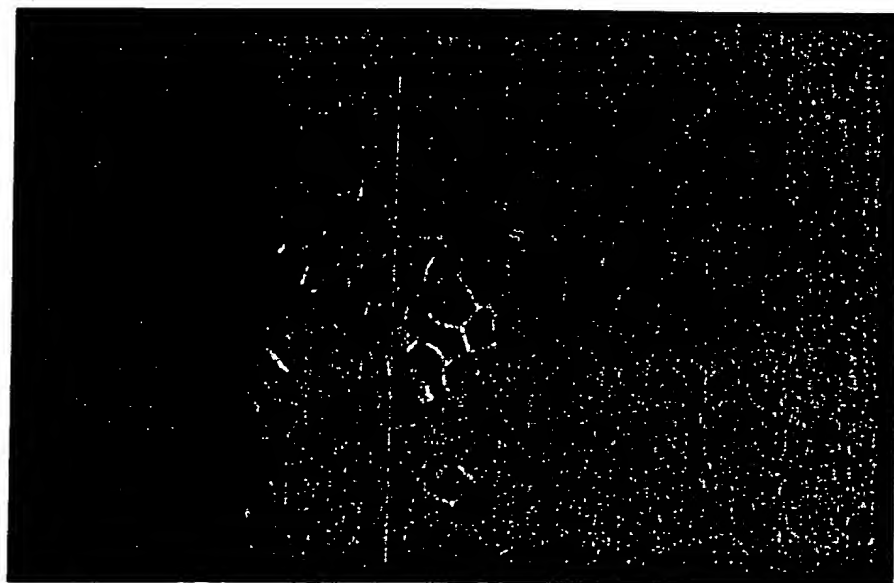
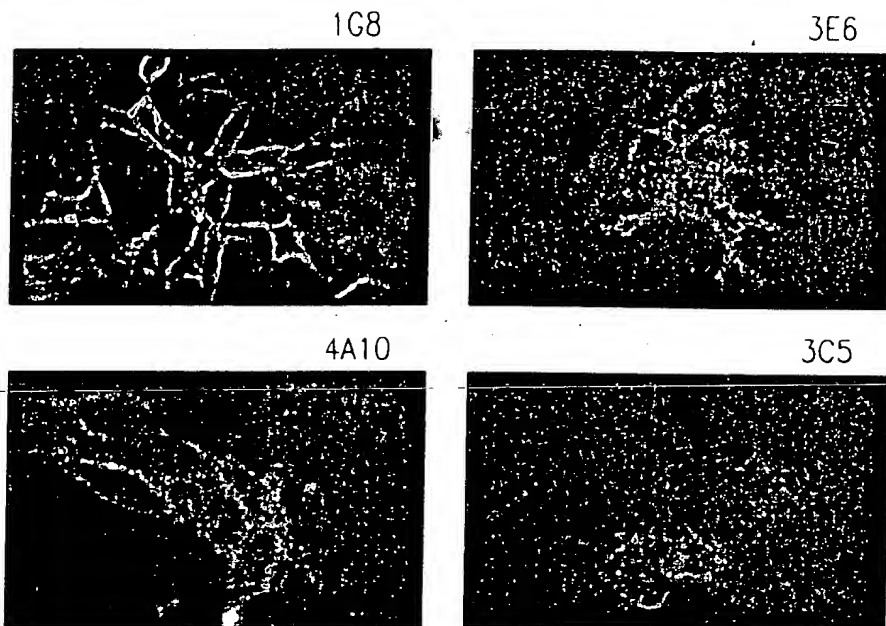


FIG. 36

09854811.072501

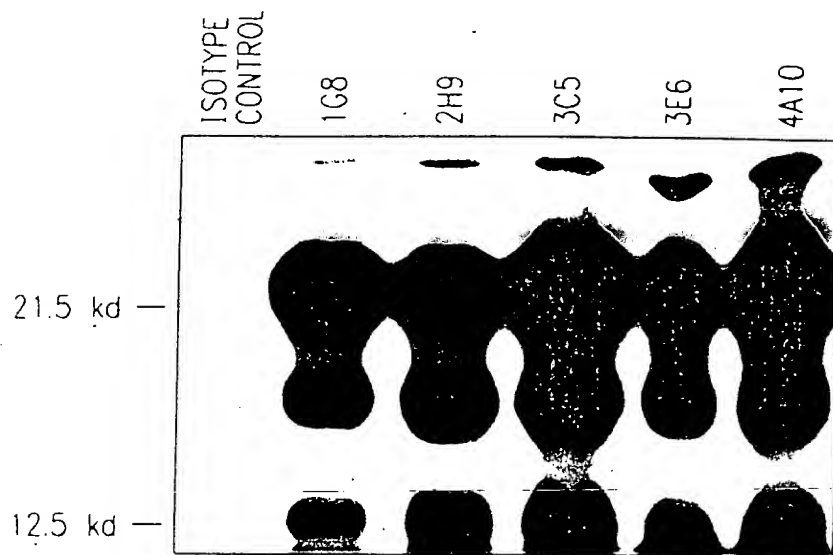


FIG. 37

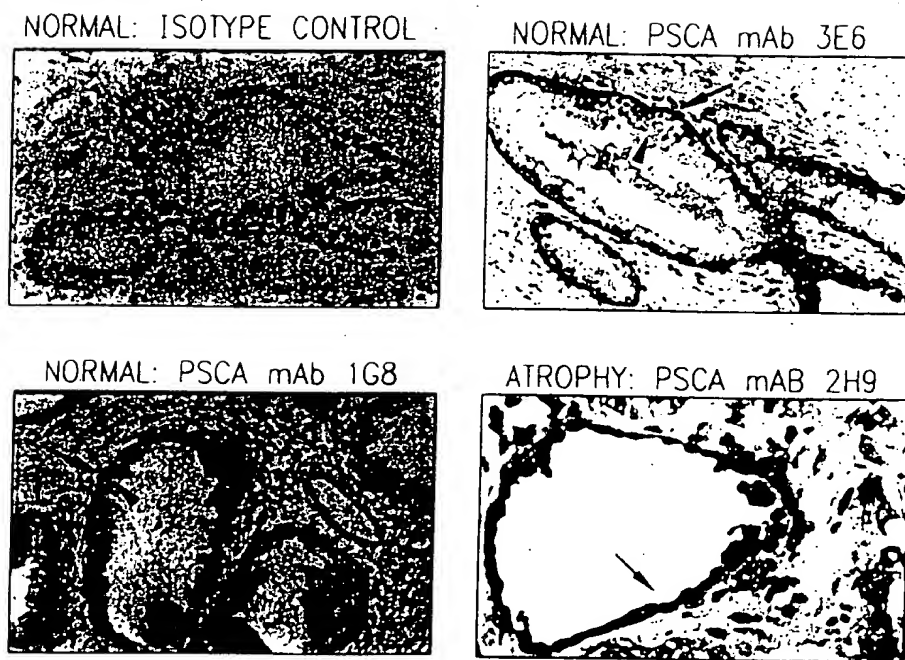
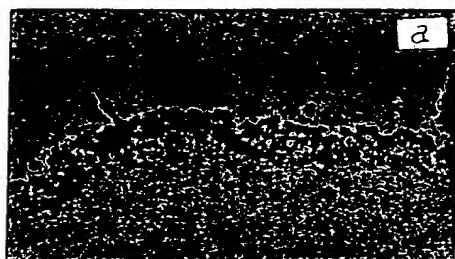
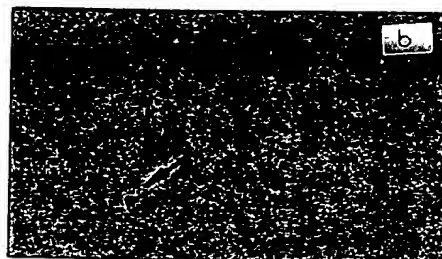


FIG. 38

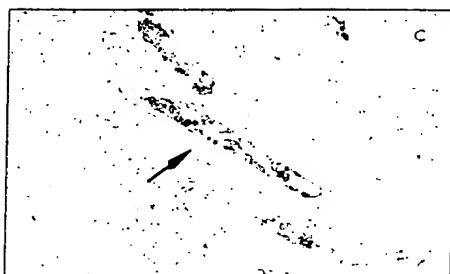
FIG. 39A



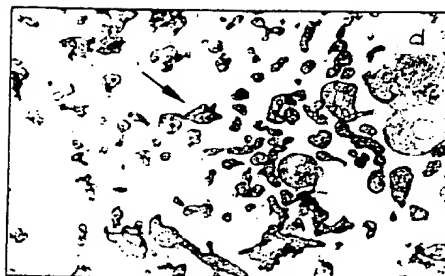
BLADDER: 1G8



COLON: 1G8



KIDNEY: 3E6



PLACENTA: 3E6

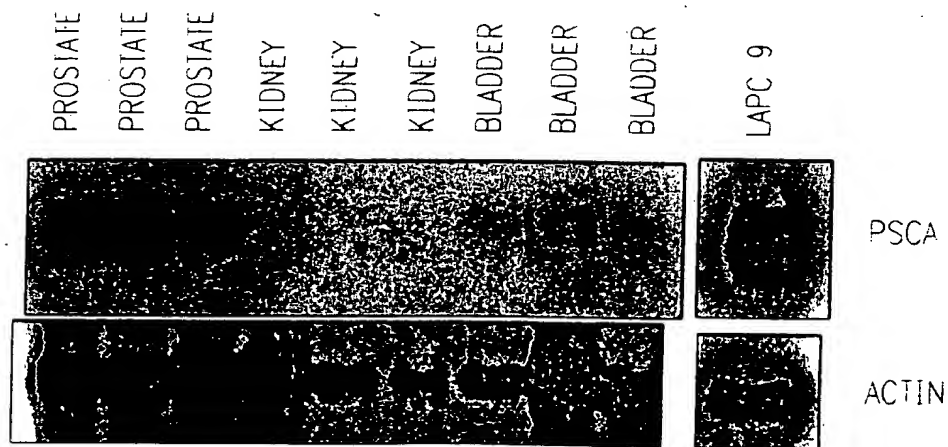


FIG. 39B

FIG. 40A

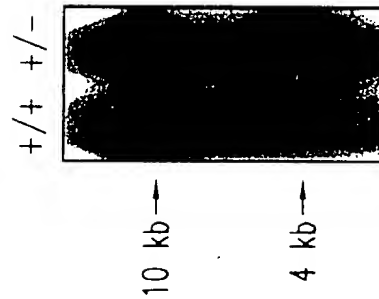
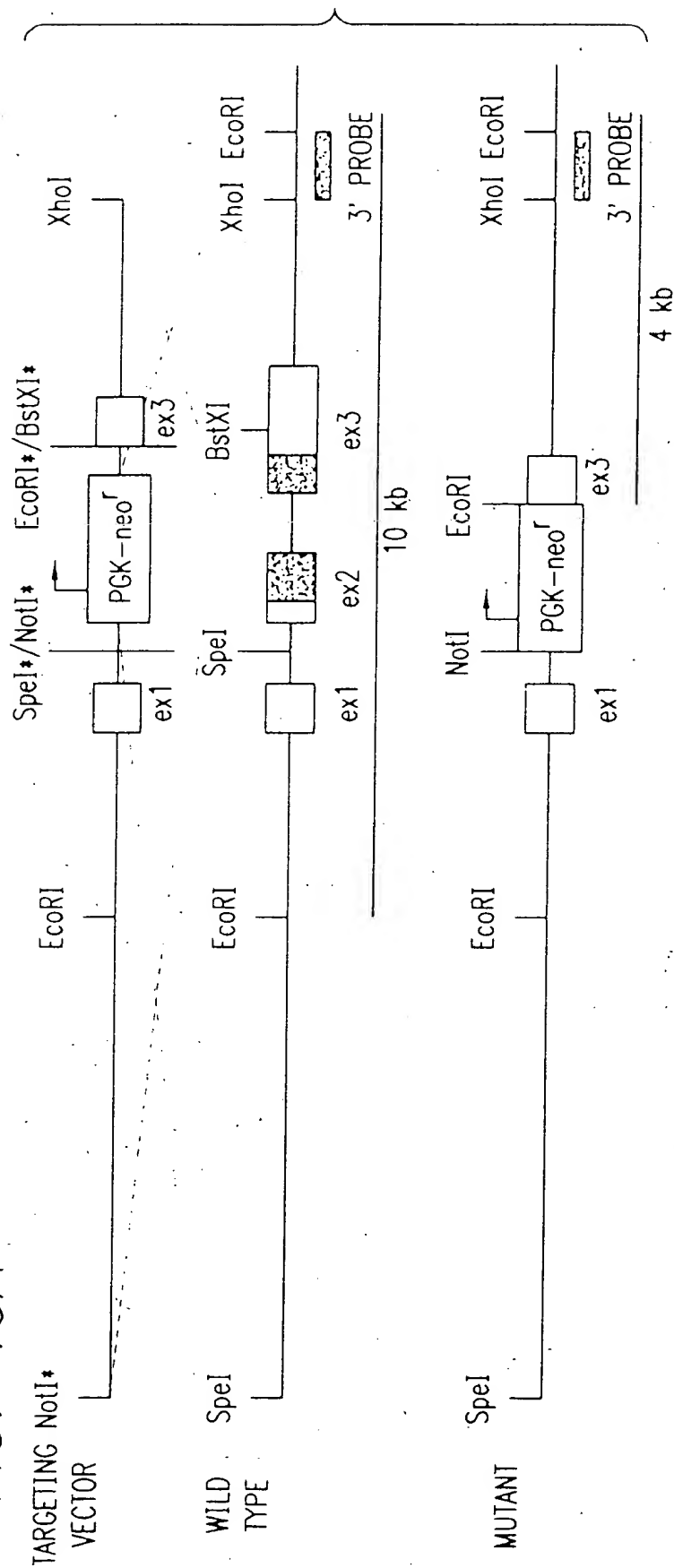
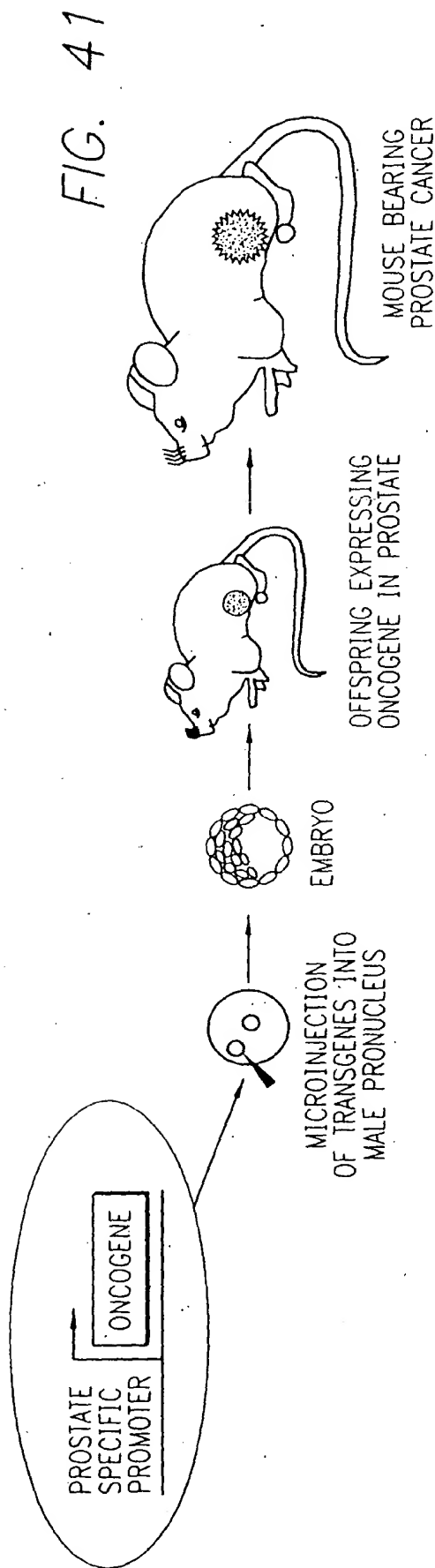


FIG. 40B



TRANSGENE	TARGET TISSUES	CHARACTERISTICS
C3(1) (-3 kb)/ SV40 LARGE+SMALL, T MAROULAKOU et al. 1994. PNAS	PROSTATE (SECRETORY CELLS) URETHRAL, MAMMARY AND SWEAT GLAND	LOW-GRADE PIN 8-12 WKS HIGH-GRADE PIN 8-12 WKS INVASIVE CARCINOMA 28 WKS NO METASTASES
PROBASIN (-426 bp)/ SV40 LARGE+SMALL, T GREENBERG et al. 1995 PNAS	PROSTATE (SECRETORY CELLS)	LOW-GRADE PIN 5-8 WKS HIGH-GRADE PIN 8-12 WKS INVASIVE CARCINOMA 12 WKS METASTASES IN LYMPH NODE, LUNG, LIVER AND BONE
CRYPTIDIN2 (-6.5 kb)/ SV40 LARGE+SMALL, T CARABEDIAN et al. 1998 PNAS	PROSTATE (NEUROENDOCRINE CELLS) SMALL INTESTINE	LOW-GRADE PIN 8-12 WKS HIGH-GRADE PIN 8-12 WKS INVASIVE CARCINOMA 16 WKS METASTASES IN LYMPH NODE, LUNG, LIVER, AND BONE

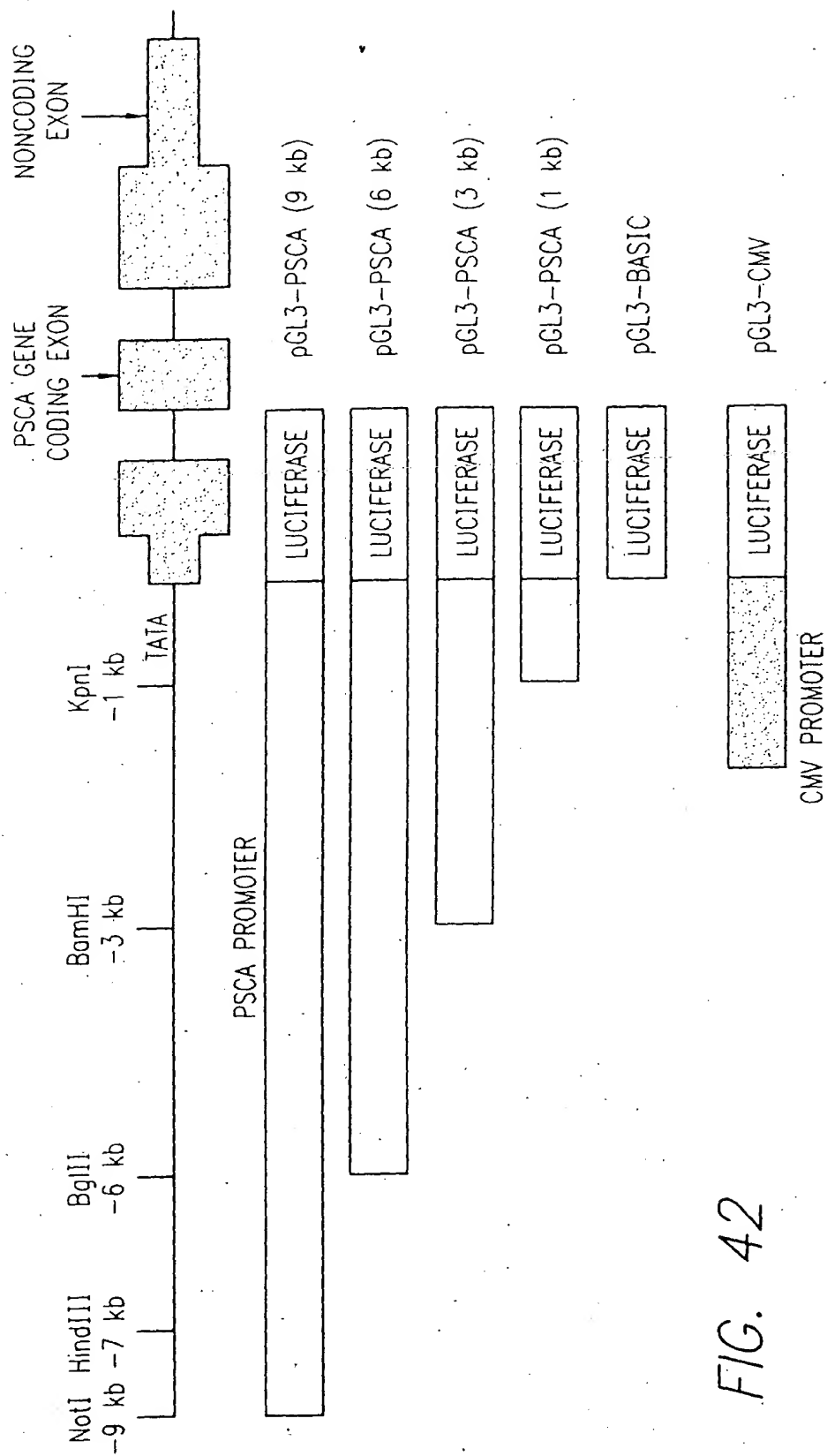


FIG. 42

FO52/0"TF845860

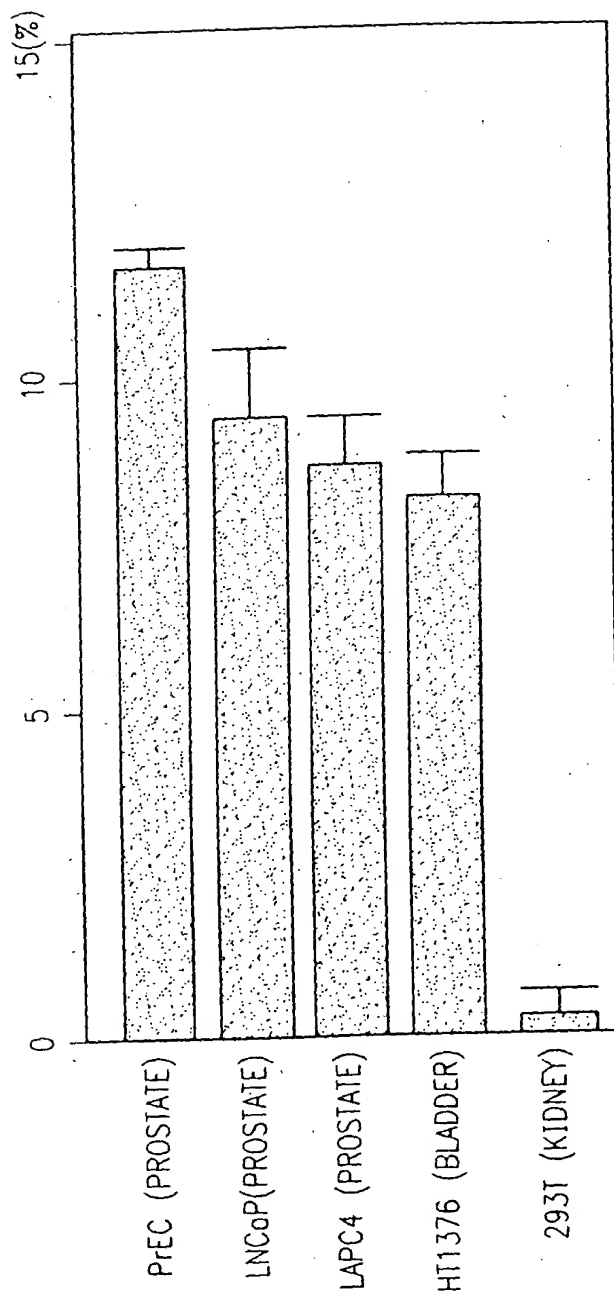


FIG. 43

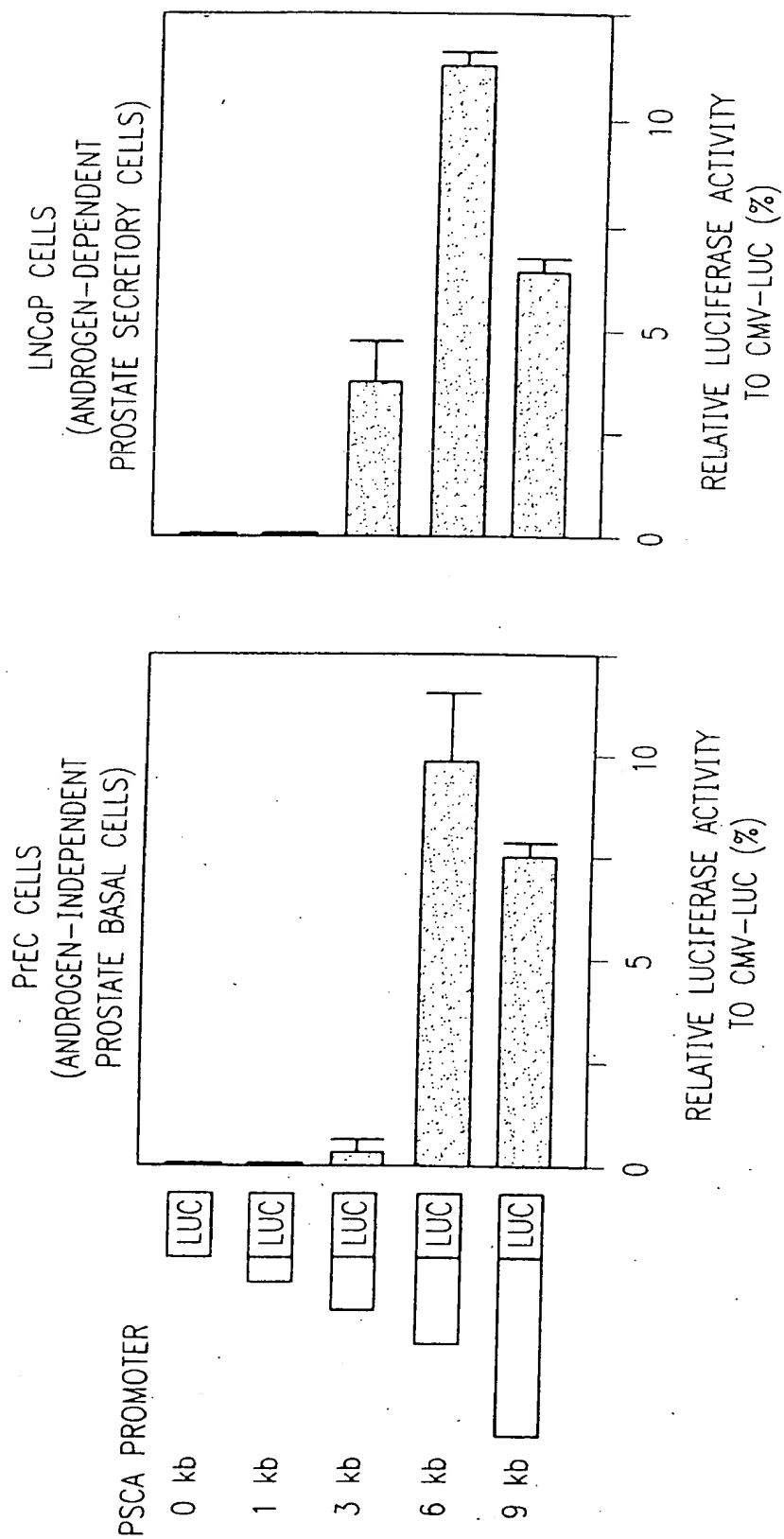
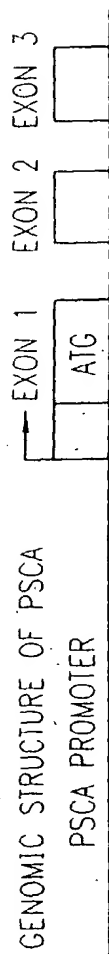


FIG. 44

FIG. 45



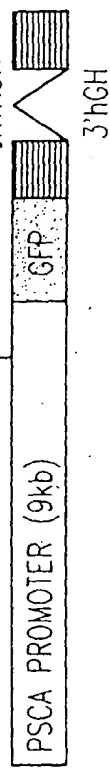
PSCA(9 kb)-GFP



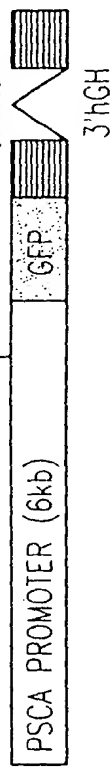
PSCA(6 kb)-GFP



PSCA(9 kb)-GFP-3'hGH



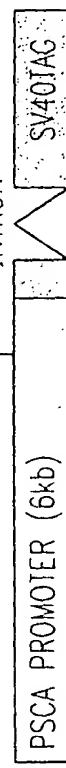
PSCA(6 kb)-GFP-3'hGH



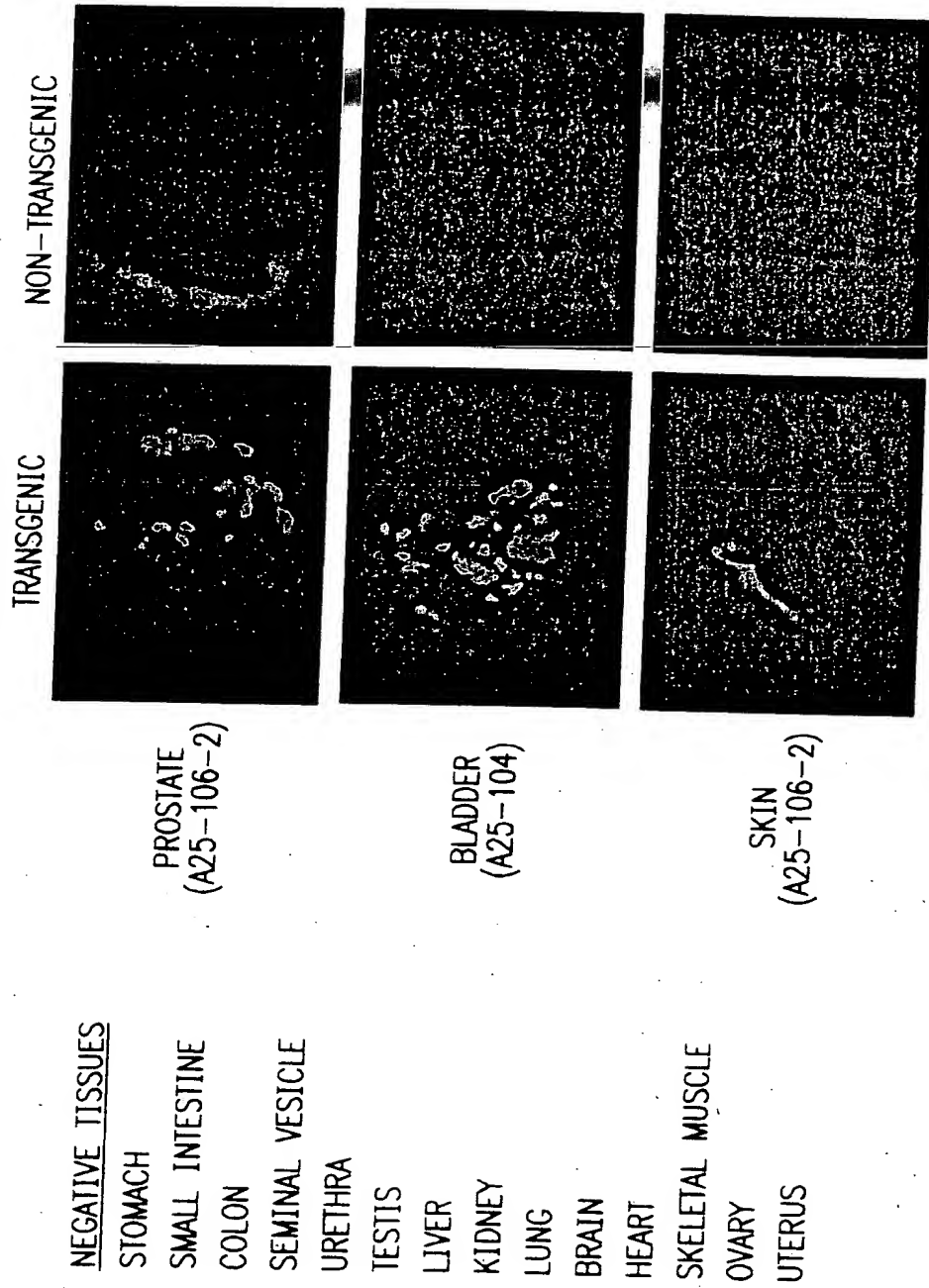
PSCA(9 kb)-SV40TAG



PSCA(6 kb)-SV40TAG



NUMBER OF FOUNDERS (DNA POSITIVE)
2
1
6
8
3
9



NEGATIVE TISSUES

STOMACH

SMALL INTESTINE

COLON

SEMINAL VESICLE

URETHRA

TESTIS

LIVER

KIDNEY

LUNG

BRAIN

HEART

SKELETAL MUSCLE

OVARY

UTERUS

FIG. 46

095431.02501

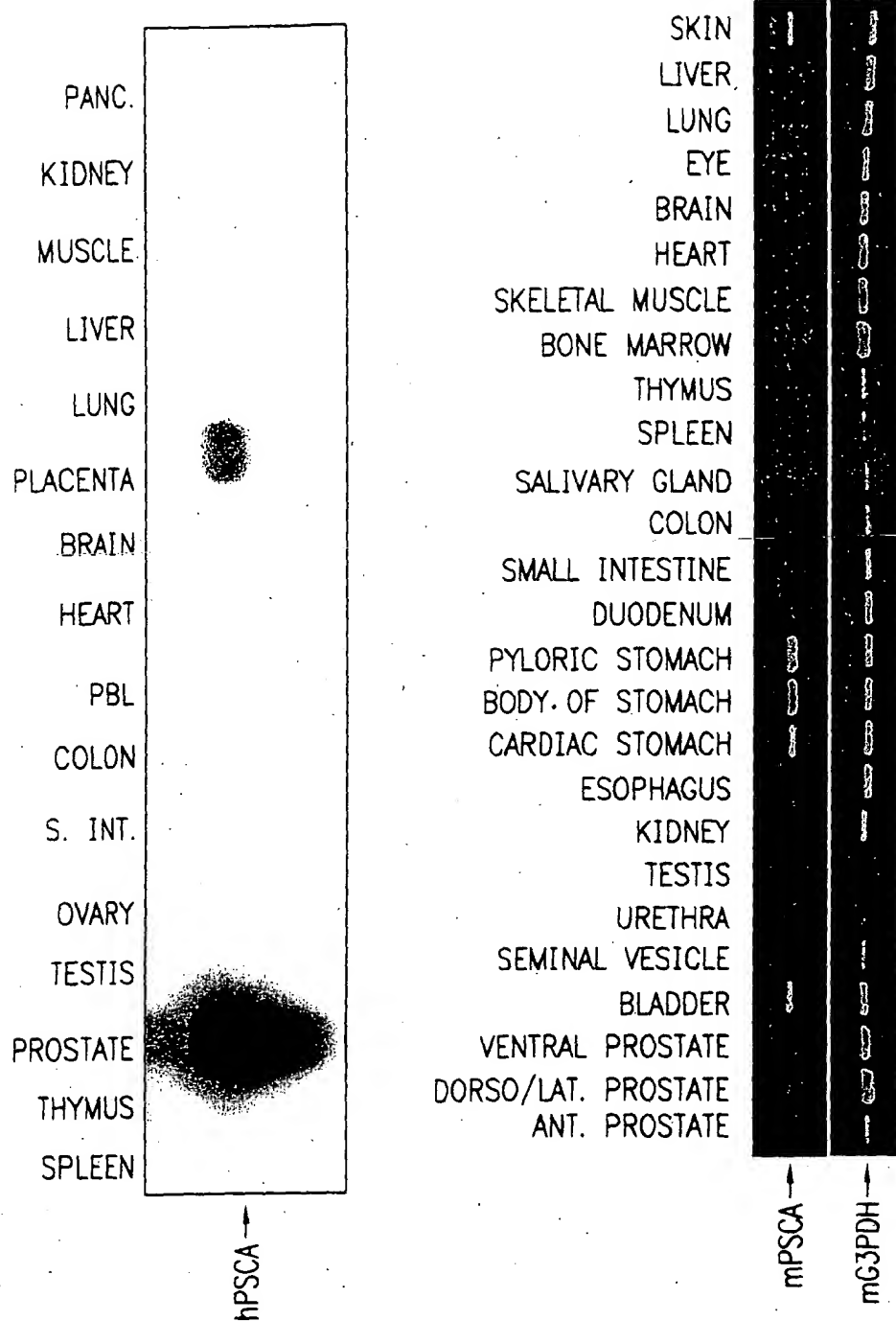


FIG. 47

058431-07501

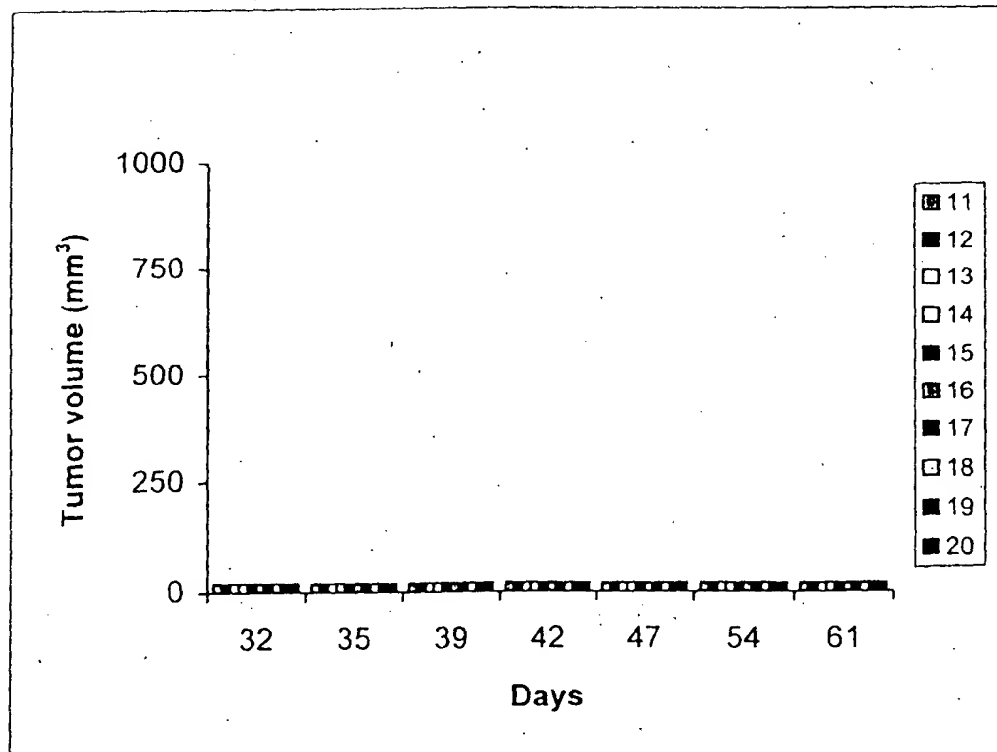
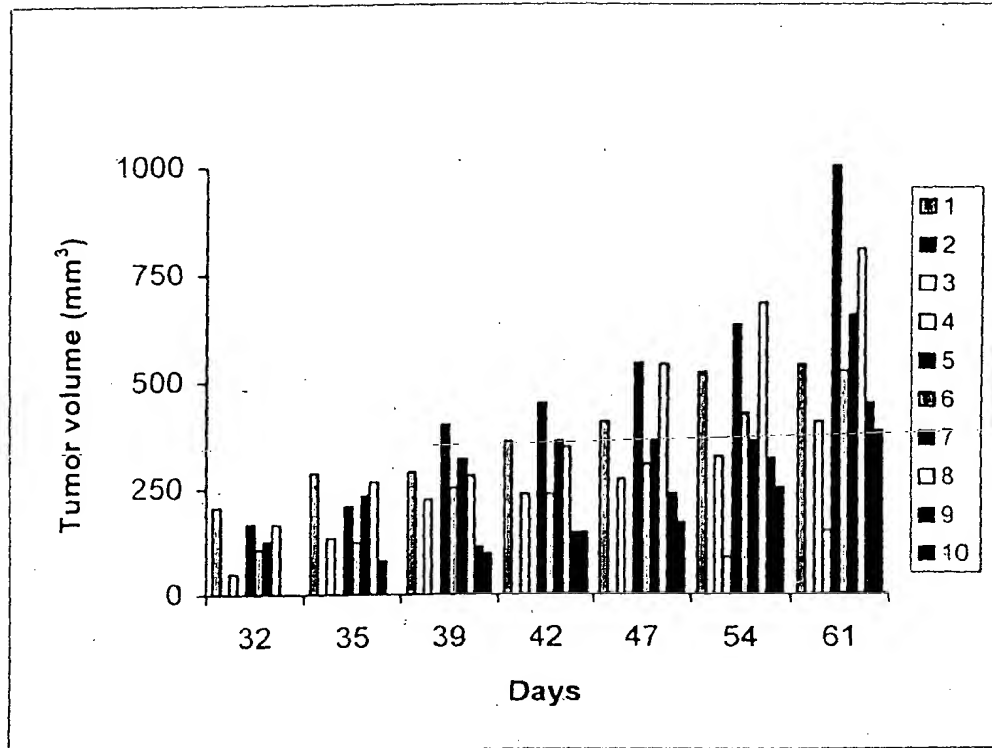


FIG. 49

A

Epitope recognized (OD 450 nm)

<u>mAb</u>	<u>Isotype</u>	<u>F (18-98)</u>	<u>N (2-50)</u>	<u>M (46-109)</u>	<u>C (85-123)</u>
1G8	IgG1 k	1.485	0.004	1.273	0.003
2A2	IgG2a k	0.973	0.631	0.023	0.010
2H9	IgG1 k	1.069	1.026	0.002	0.001
3C5	IgG2a k	1.916	1.709	0.006	0.002
3E6	IgG3 k	1.609	0.036	1.133	2.118
3G3	IgG2a k	2.805	1.731	0.004	0.000
4A10	IgG2a k	1.053	0.493	0.000	0.001

B

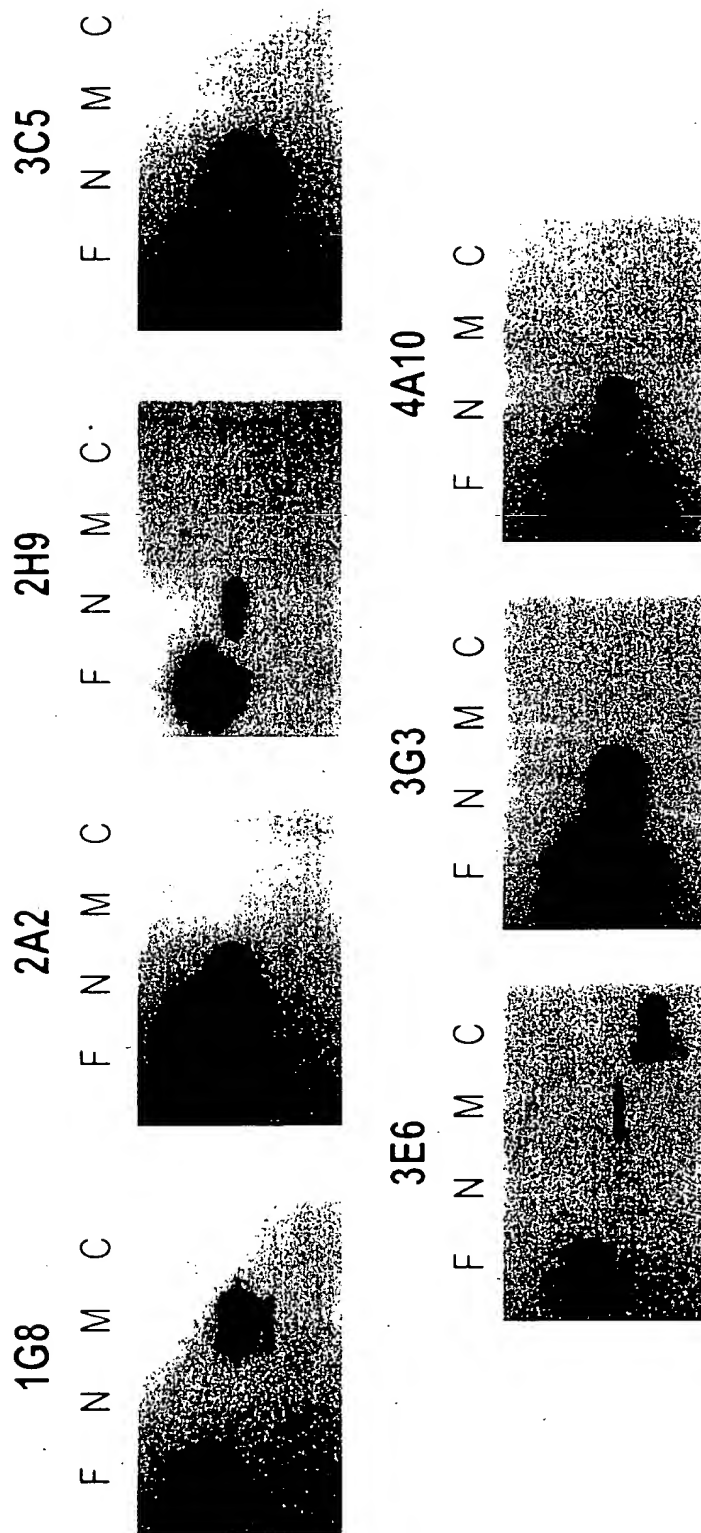
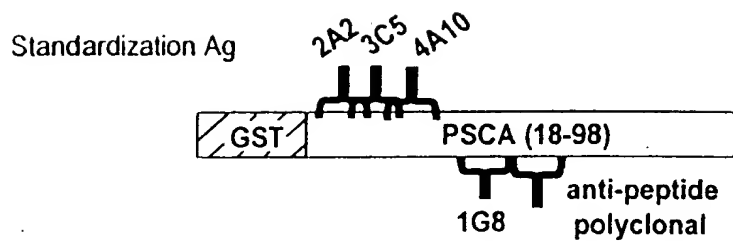
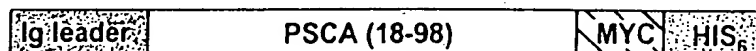


FIG. 50

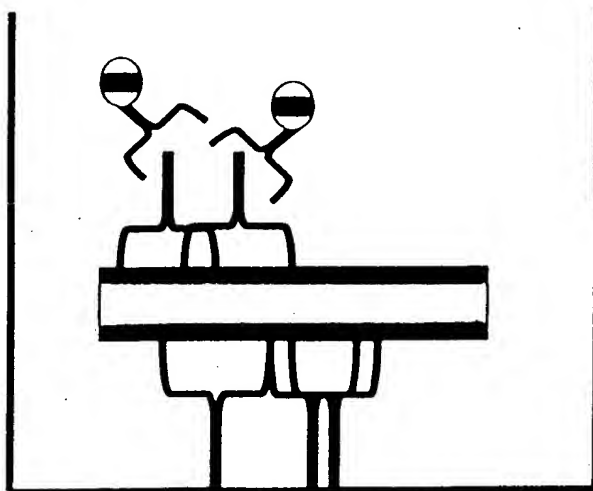
A



Engineered mammalian secreted form



B



Anti-IgG2a HRP

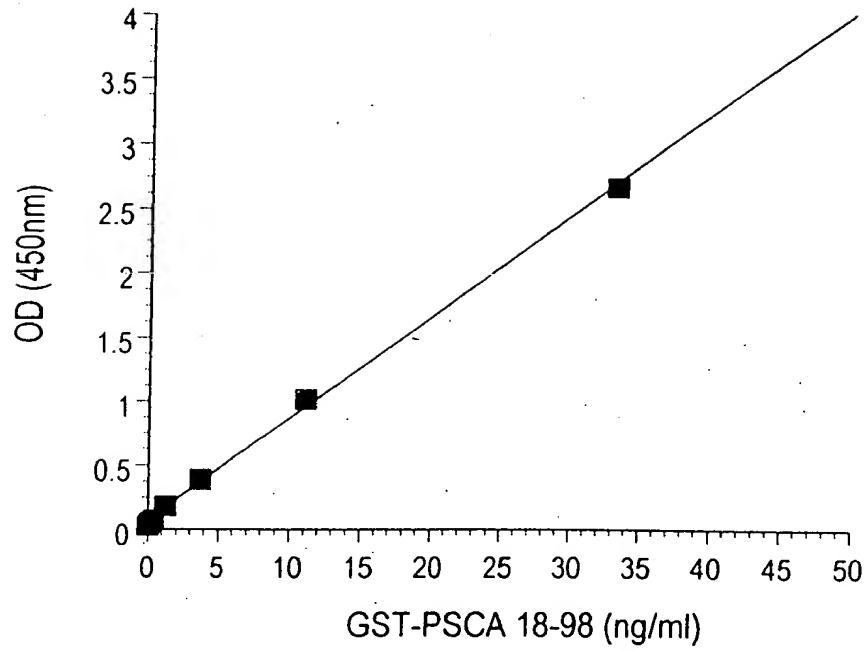
Anti-PSCA mAbs 3C5+4A10+2A2 (IgG2a)

PSCA

Affinity purified anti-peptide polyclonal
+ mAb 1G8 (IgG1)

FIG. 51

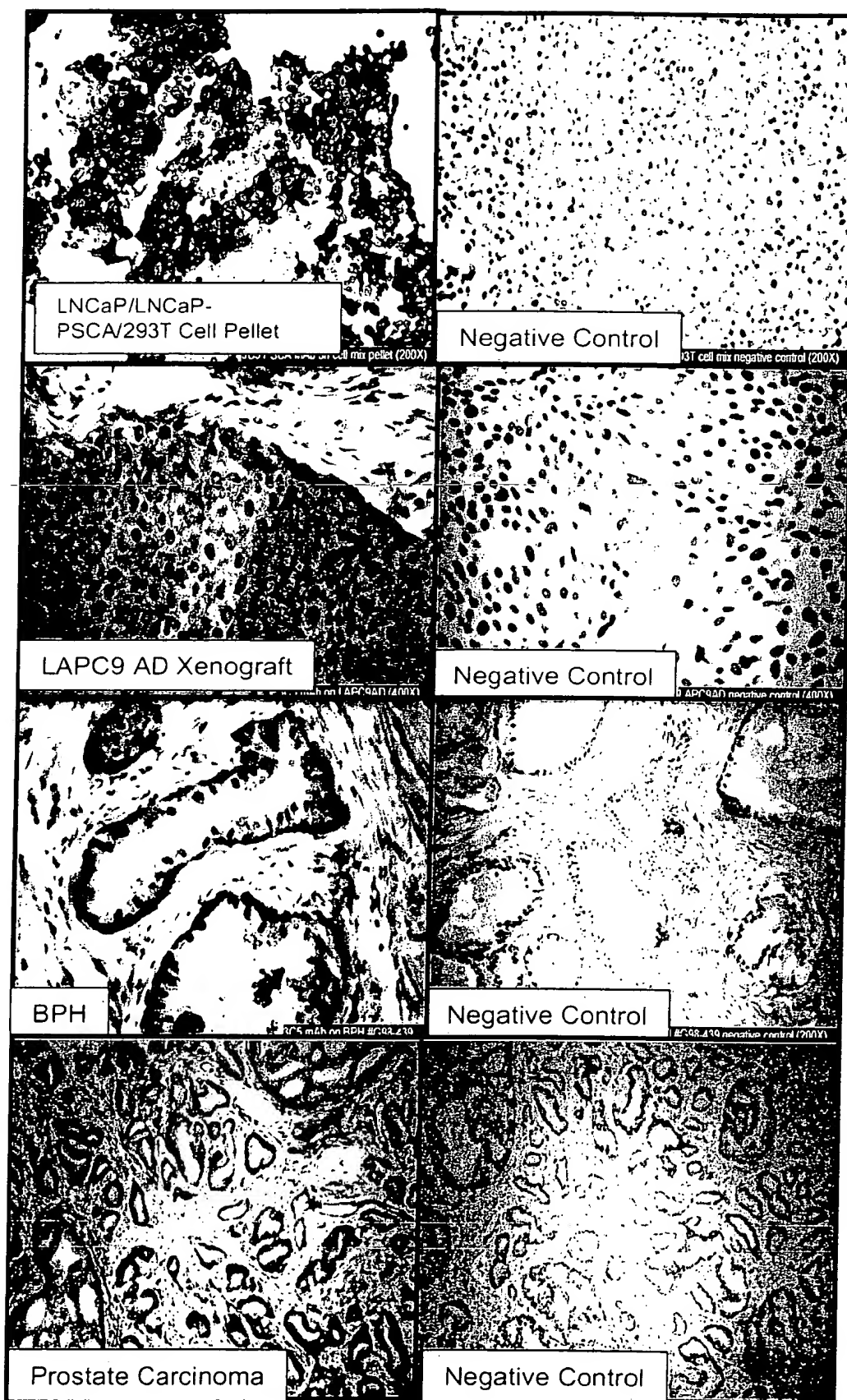
A



B

Sample	OD+range (n=2)	ng/ml
vector	0.005+0.001	ND
vector+hu serum	0.004+0.001	ND
secPSCA	2.695+0.031	32.92
secPSCA+hu serum	2.187+0.029	26.55

FIG. 52



09854811.072501

FIG. 53

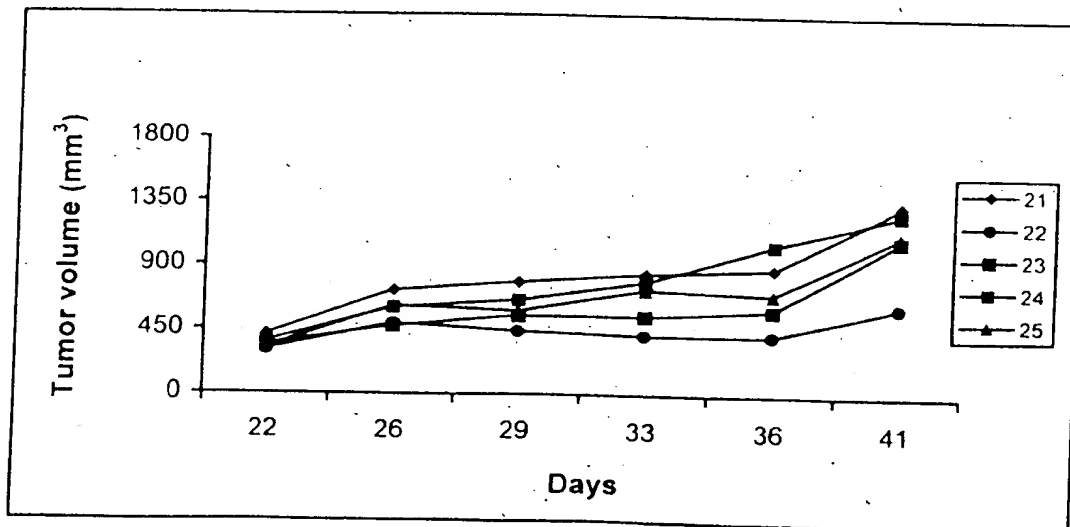
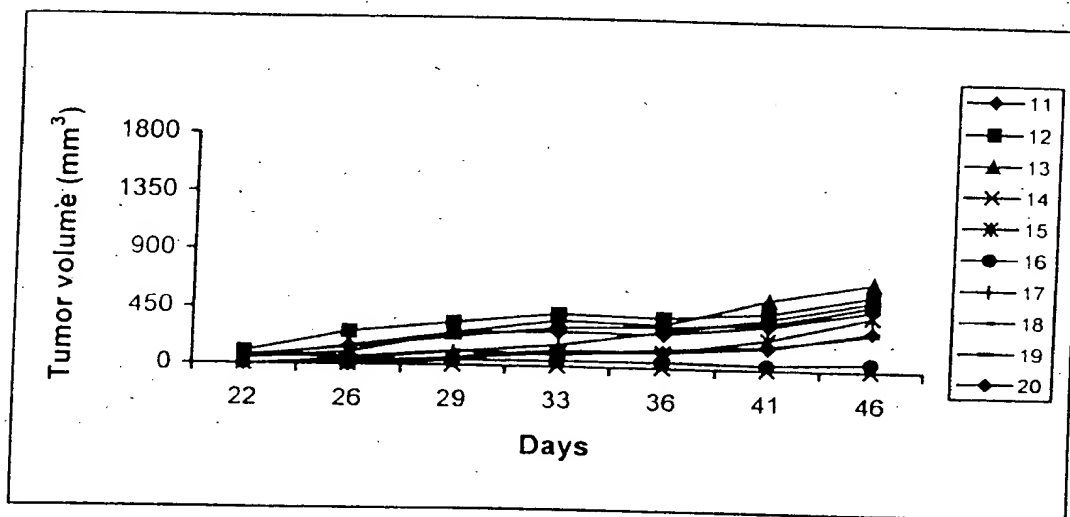
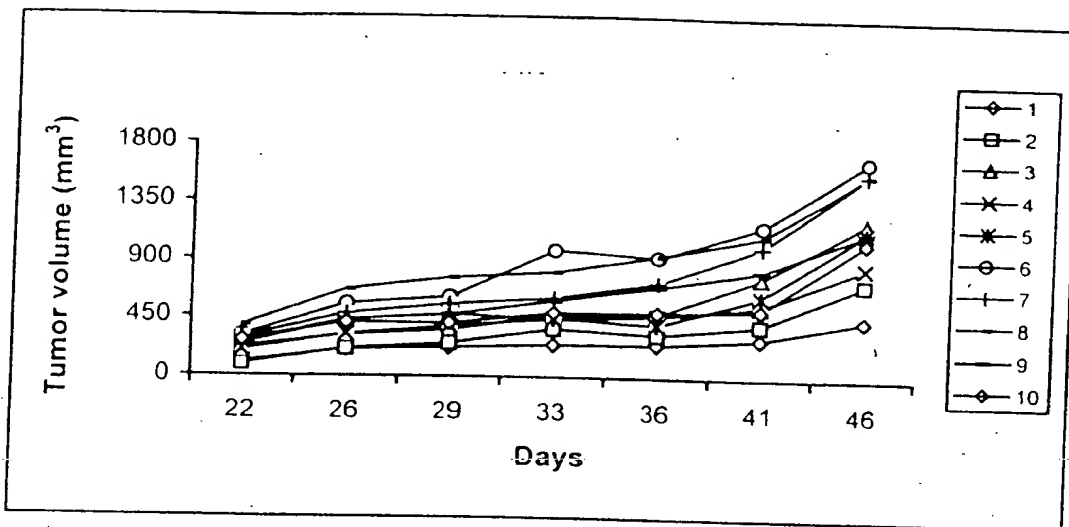


FIG. 54

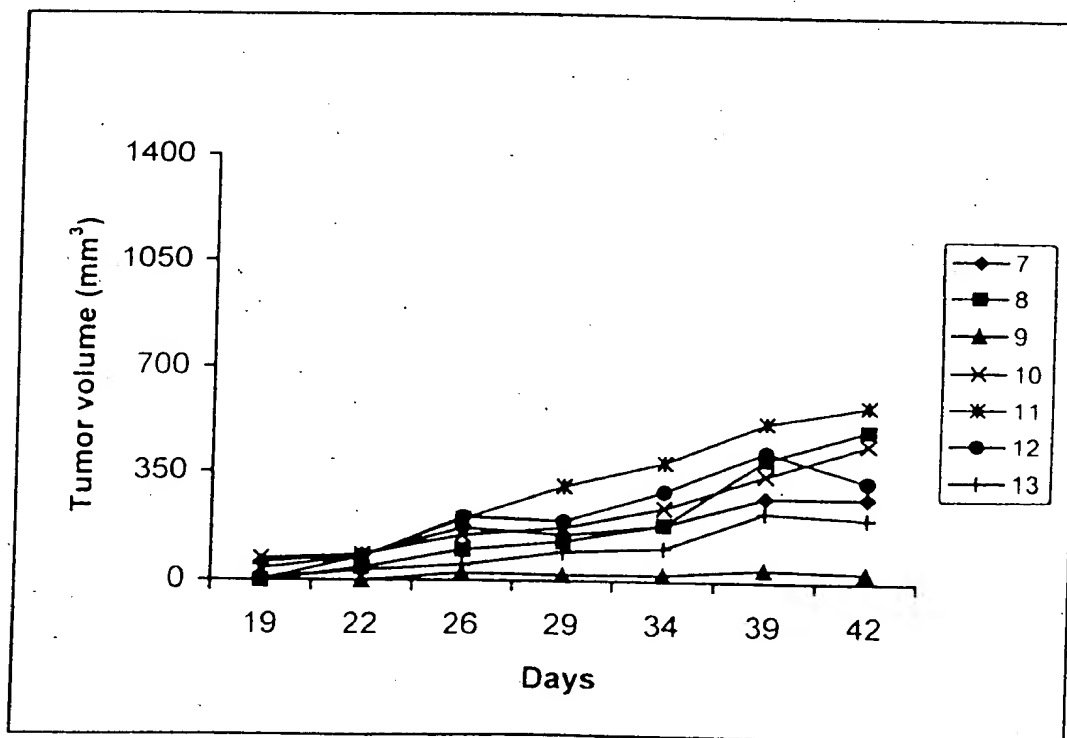
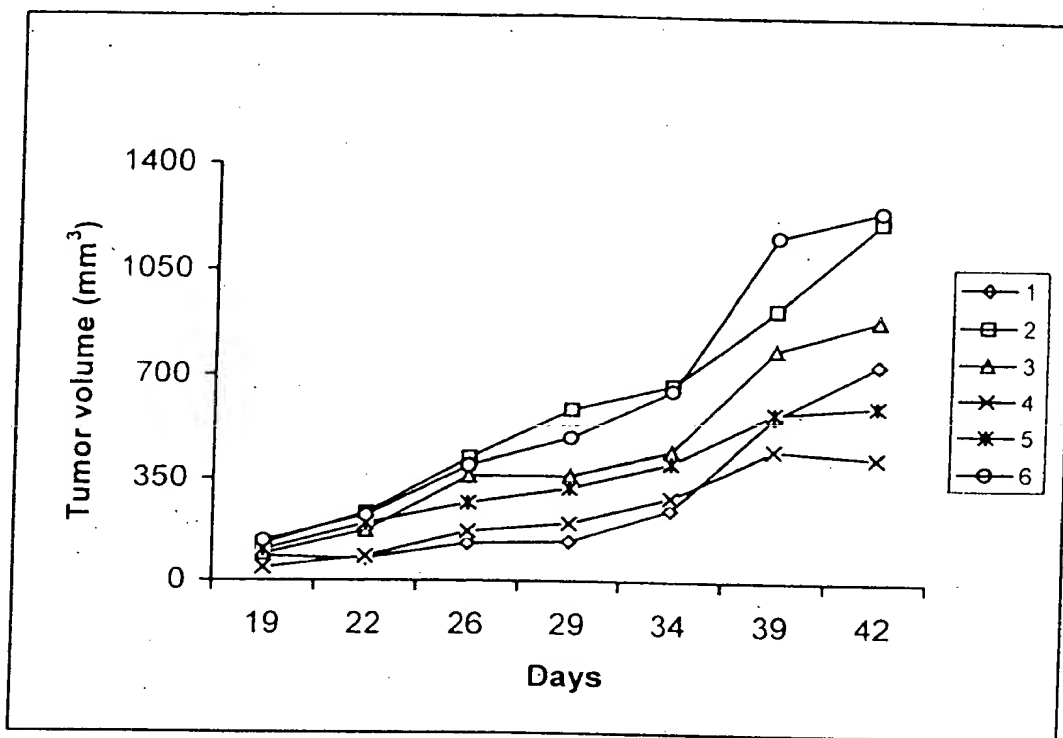


FIG. 55

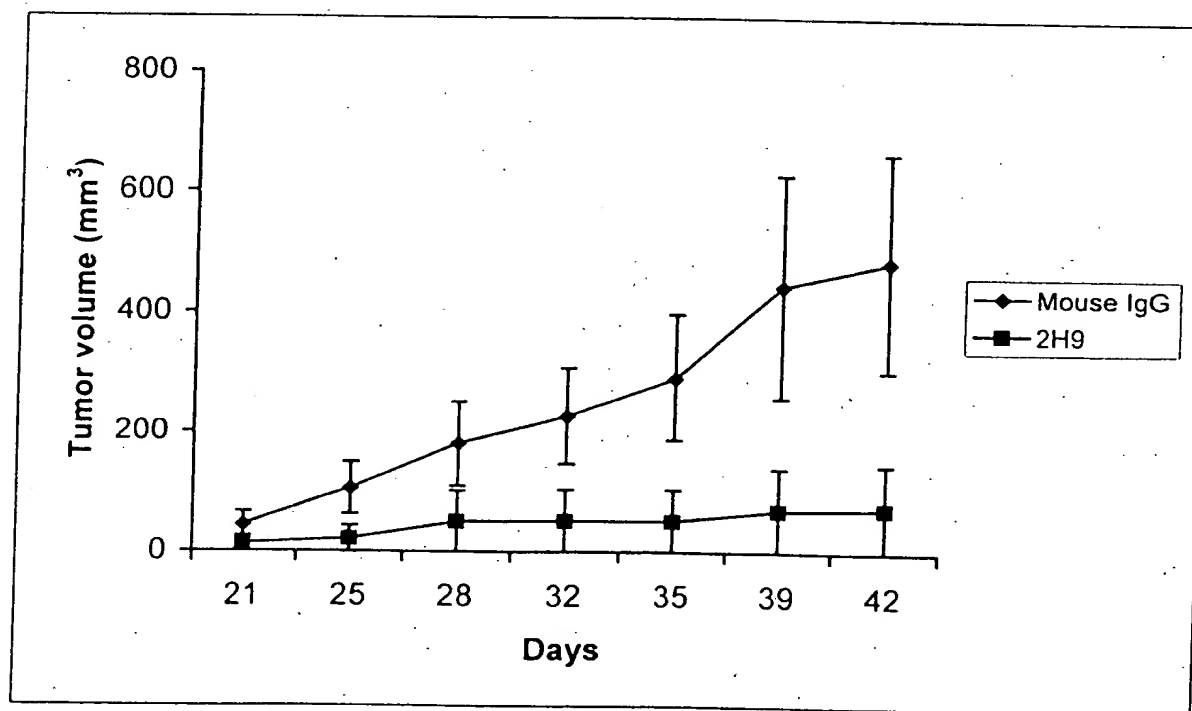
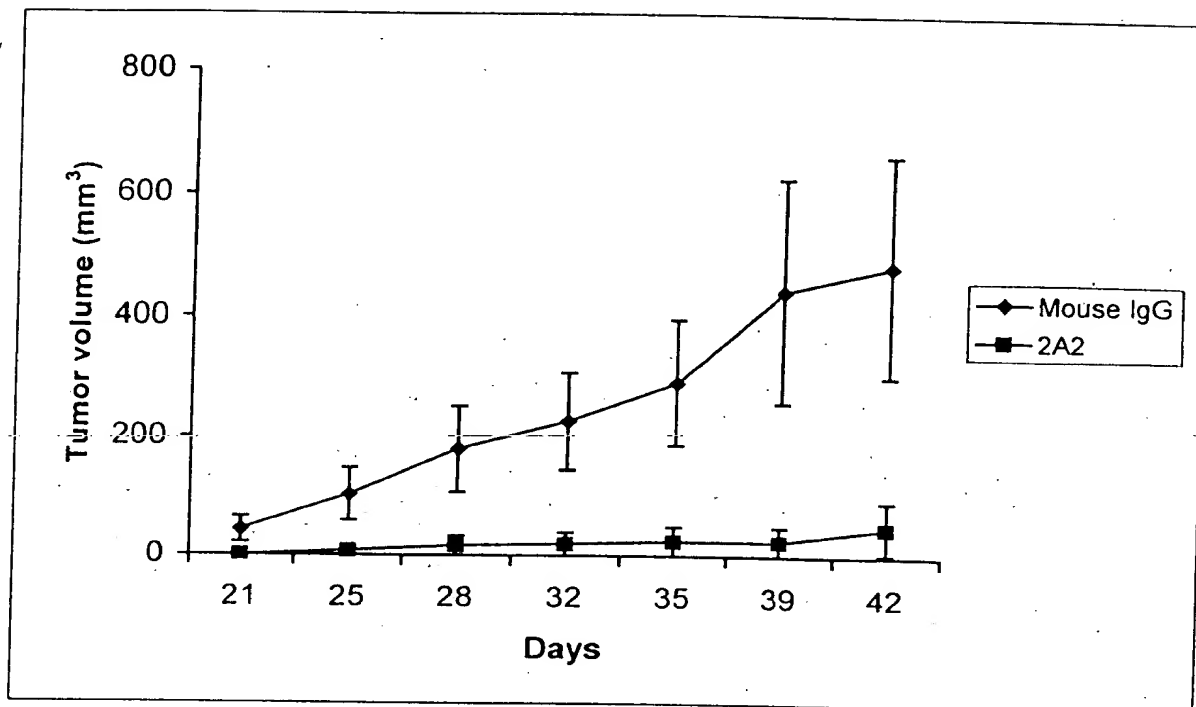
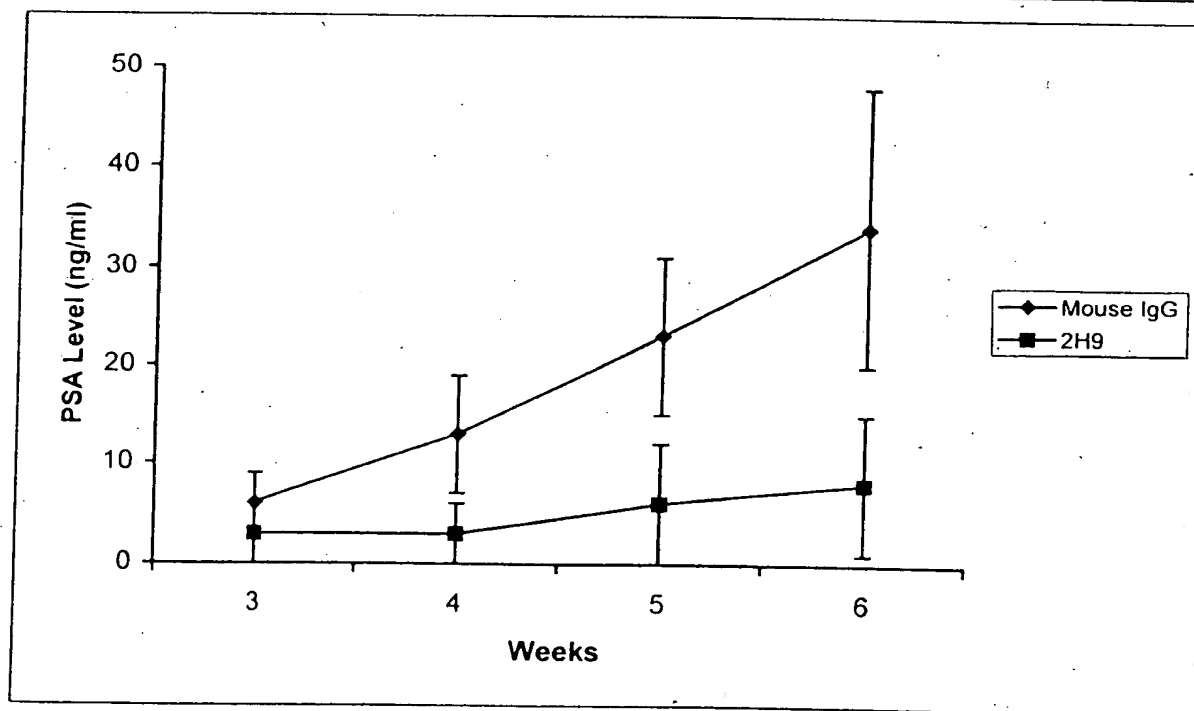
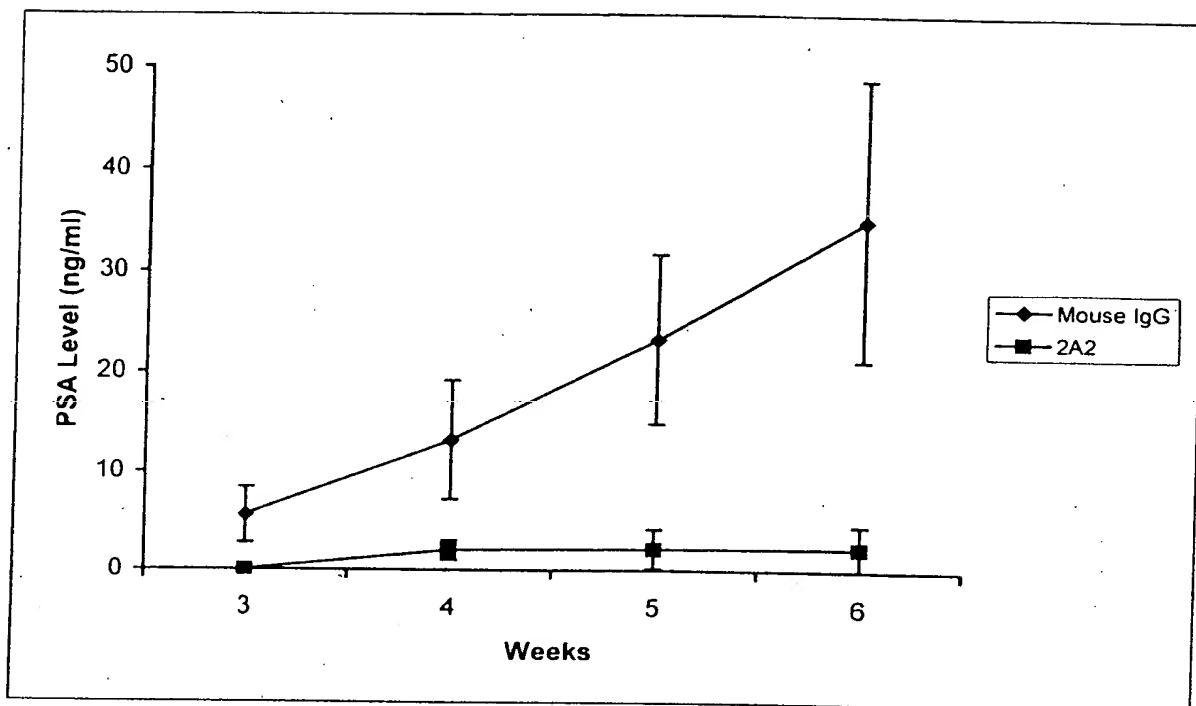


FIG. 56



0985481.02501
T05270" T7845860

FIG. 57

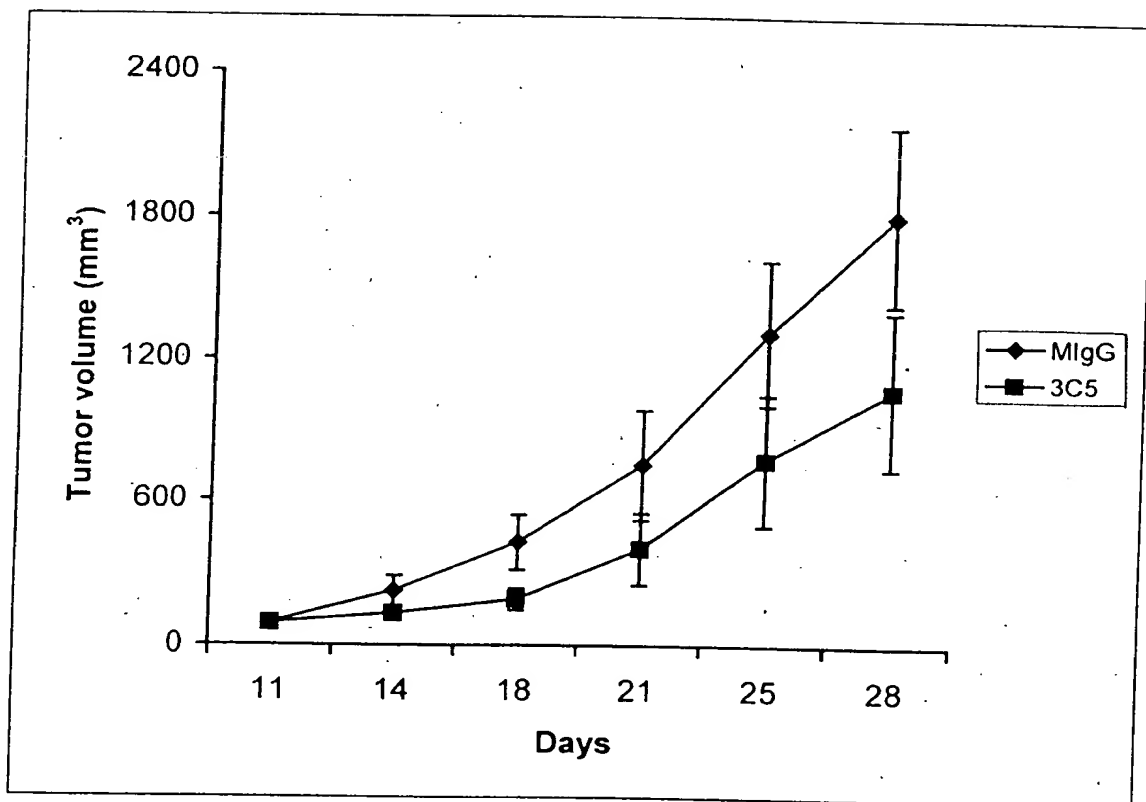


FIG. 58

TGCTTCTTCCTGATGGCAGTGGTTATAGGAGTCAATTACAGAGGTTACGCTGCAGCAGTCT 60
 C F F L M A V V I G V N S E V Q L Q Q S 20

 GGGGCAGAACTTGTGAGGTCAGGGCCCTCAGTCAAGTTGTCTGACACAGCTTCTGGCTTC 120
 G A E L V R S G A S V K L S C T A S G F 40

 CDR1
 AACATTAAAGACTACTATATACACTGGGTGAATCAGAGGCCCTGACCAGGGCCTGGAGTGG 180
 N I K D Y Y I H W V N Q R P D Q G L E W 60

 CDR2
 ATTGGATGGATTGATCCTGAGAATGGTGACACTGAATTTGTCCCGAAGTTCAGGGCAAG 240
 I G W I D P E N G D T E F V P K F Q G K 80

 GCCACTATGACTGCAGACATTTTCTCCAACACAGCCCTACCTGCACCTCAGCAGCCTGACA 300
 A T M T A D I F S N T A Y L H L S S L T 100

 CDR3
 TCTGAAGACACTGCCGTCTATTACTGTAAACGGGGGTTTCTGGGGCCCAAGGACTCTG 360
 S E D T A V Y Y C K T G G F W G Q G T L 120

 GTCACGTCTCTGCAGCCAAAACGACACCCCATCTGTCTATCCACTG
 V T V S A A K T T P P S V Y P L

FIG. 59

TTGGTAGCAACAGCCTCAGATGTCCACTCCAGTGCCAACTGCAGCAACCTGGGTCTGAA 60
L V A T A S D V H S Q V Q L Q Q P G S E 20

CTGGTGAGGCCCTGGAACTTCAGTGAAGCTGTCTCCTGCAAGGCTTCTGGCTATACATTCTCC 120
L V R P G T S V K L S C K A S G Y T F S 40
CDR1

AGCTACTGGATGCACCTGGGTGAAGCAGAGGCCCTGGACAAGGCCTTGAGTGGATTGGAAT 180
S Y W M H W V K Q R P G Q G L E W I G N 60

ATTGACCCTGGTAGTGGTTACACTAACTACGCTGAGAACCTCAAGACCAAGGCCACACTG 240
I D P G S G Y T N Y A E N L K T K A T L 80
CDR2

ACTGTAGACACATCCTCCAGCACAGCCTACATGCAGCTCAGCAGCCTGACATCTGAGGAC 300
T V D T S S S T A Y M Q L S S L T S E D 100

TCTGCAGTCTATTACTGTACAAGCCGATCTACTATGATTACGACGGGATTGCTTACTGG 360
S A V Y Y C T S R S T M I T T G F A Y W 120
CDR3

GGCCAAGGGACTCTGGTCACTGTCTCTGCAGCTACAACAACAGCCCCATCTGTCTATCCA 420
G Q G T L V T V S A A T T A P S V Y P 160

CTGGCC
L A

FIG. 60

AATGACTTCGGGTTGAGCTGGGTTTTTATTATTATTGTTCTTTTAAAGGGTCCGGAGTGAA 60
N D F G L S W V F I I V L L K G V R S E 20

GTGAGGCTTGAGGAGTCTGGAGGAGGCTGGGTGCAACCTGGAGGATCCATGAACCTCTCC 120
V R L E E S G G G W V Q P G G S M K L S 40

TGTGTAGCCTCTGGATTACTTTTCAGTAATTACTGGATGACTTGGTCCGCCAGTCTCCA 180
C V A S G F T F S N Y W M T W V R Q S P 60
CDR1

GAGAAGGGCTTGAGTGGGTTGCTGAAATTCGATTGAGATCTGAAAATTATGCAACACAT 240
E K G L E W V A E I R L R S E N Y A T H 80
CDR2

TATCGGAGTCTGTGAAAGGGAATTACCATCTCAAGAGATGATTCAGAAAGTGTCTC 300
Y A E S V K G K F T I S R D D S R S R L 100

TACCTGCAAAATGAACAACCTTAAGACCTGAAGACAGTGAATTATTACTGTACAGATGGT 360
Y L Q M N N L R P E D S G I Y Y C T D G 120

CTGGGACGACCTAACTGGGGCCAAGGACTCTGGTCACTGTCTCTGACGCCAAACGACA 420
L G R P N W G Q G T L V T V S A A K T T 140
CDR3

CCCCATCTGTCTATCCACTGGCCCCCTTGTA
P P S V Y P L A P C V

FIG. 61

CDR1 Comparisons

1G8	1gG _{1k}	Middle	G	F	N	I	K	D	Y	Y	I	H
2H9	1gG _{1k}	N-Term.	G	F	T	F	S	N	Y	W	M	T
4A10	1gG _{2ak}	N-Term.	G	Y	T	F	S	S	Y	W	M	H

CDR2 Comparisons

1G8	1gG _{1k}	W	I	D	P	E	N	G	D	T	E	F	V	P	K	F	Q	G		
2H9	1gG _{1k}	E	I	R	L	R	S	E	N	Y	A	T	H	Y	A	E	S	V	K	G
4A10	1gG _{2ak}	N	I	D	P	G	S	G	Y	T	N	Y	A	E	N	L	K	T		

CDR3 Comparisons

1G8	1gG _{1k}	G	G	F													
2H9	1gG _{1k}	L	G	R	P	N											
4A10	1gG _{2ak}	R	S	T	M	I	T	T	G	F	A	Y					

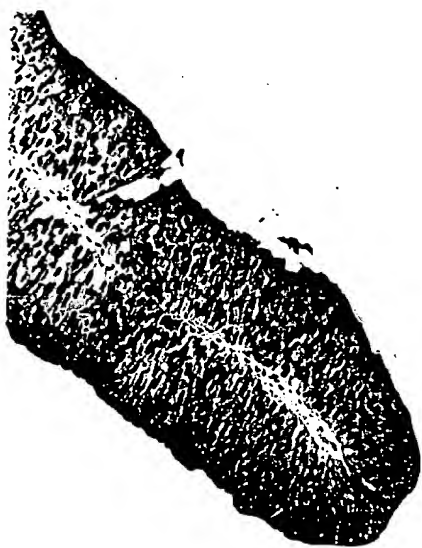
0985491.072501

FIG. 62

A



B



C



D



09854811.072504

FIG. 63

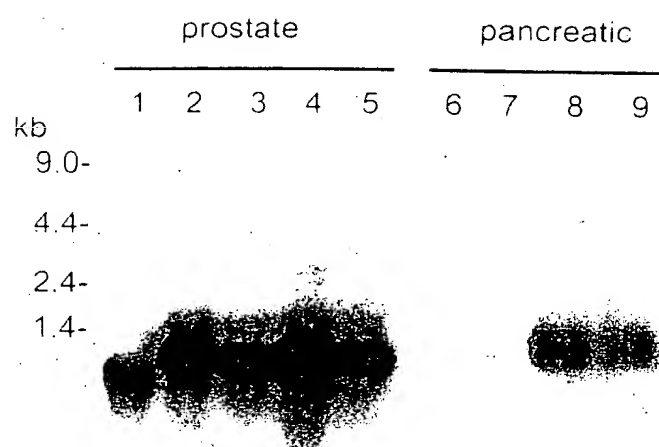


FIG. 64

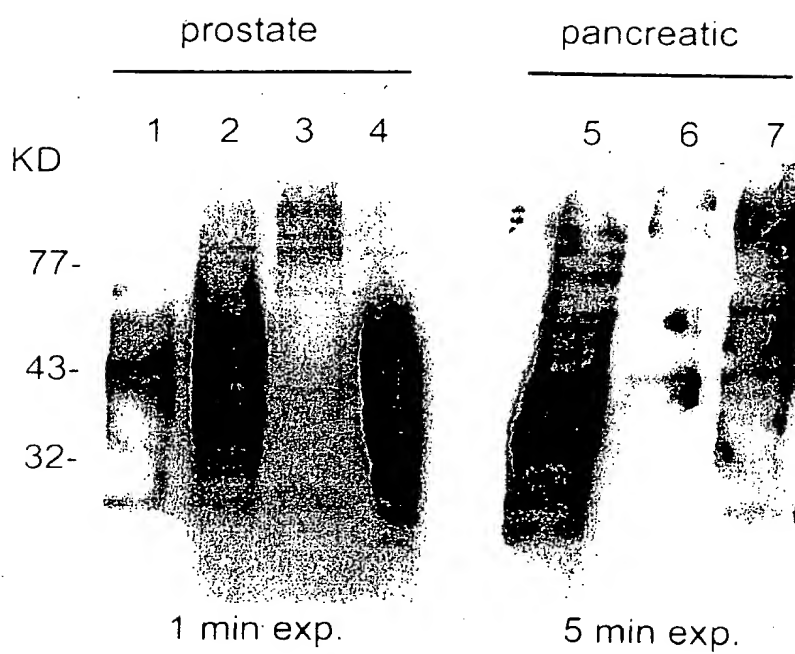


FIG. 65

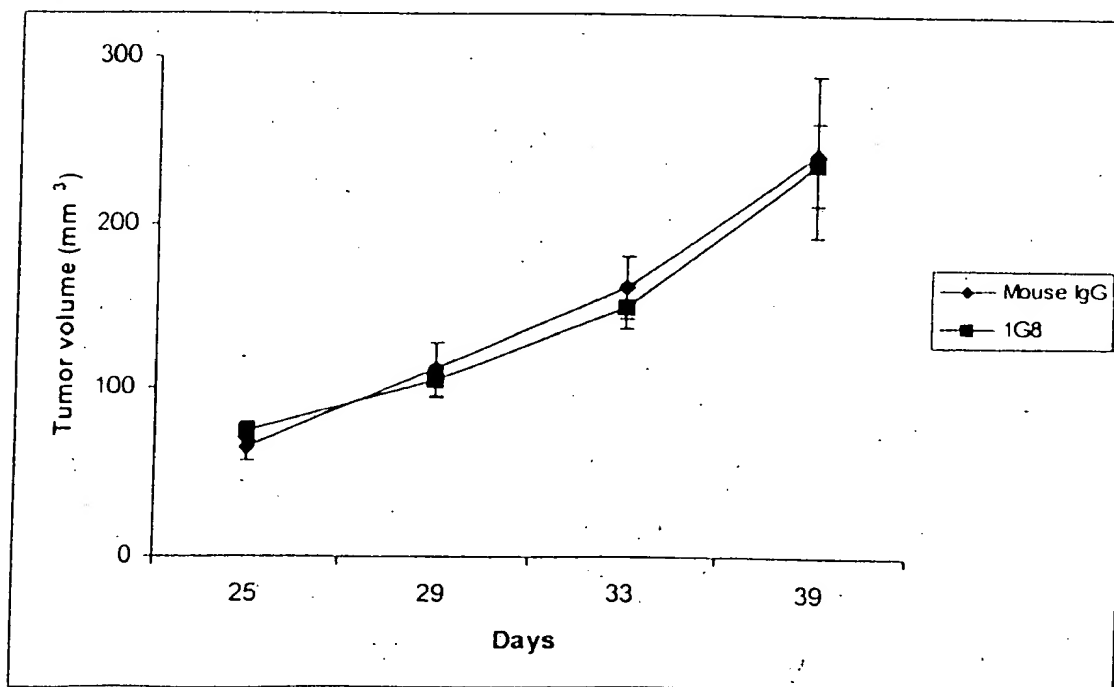
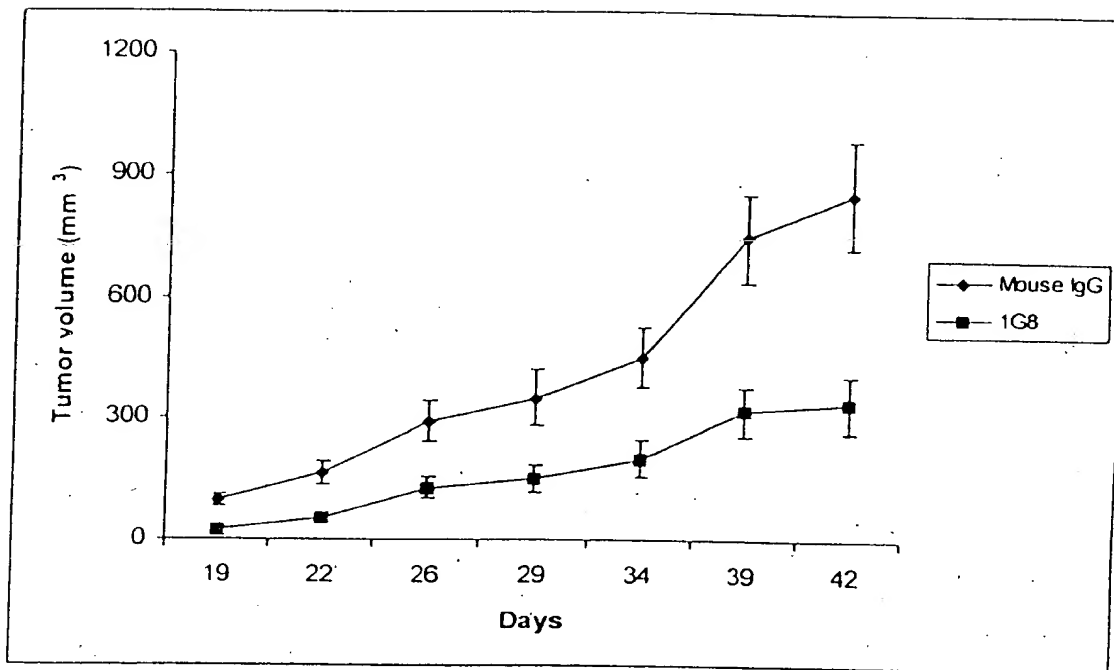
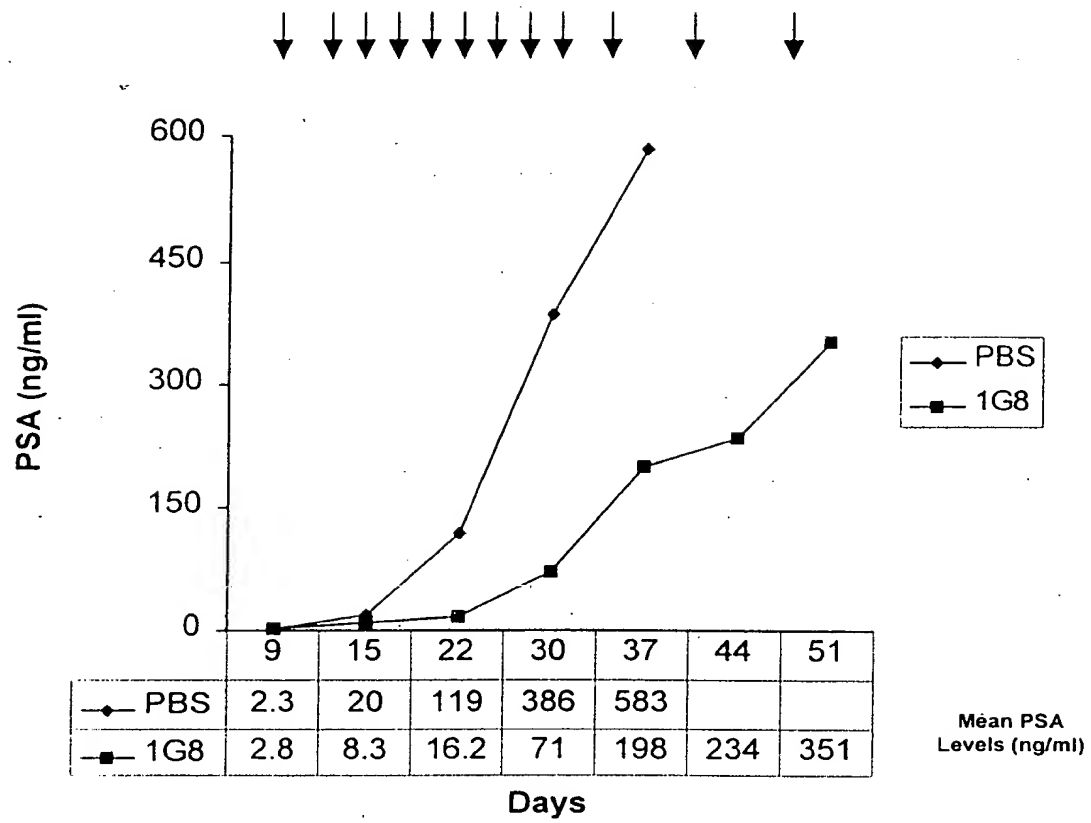


FIG. 66

A)



B)

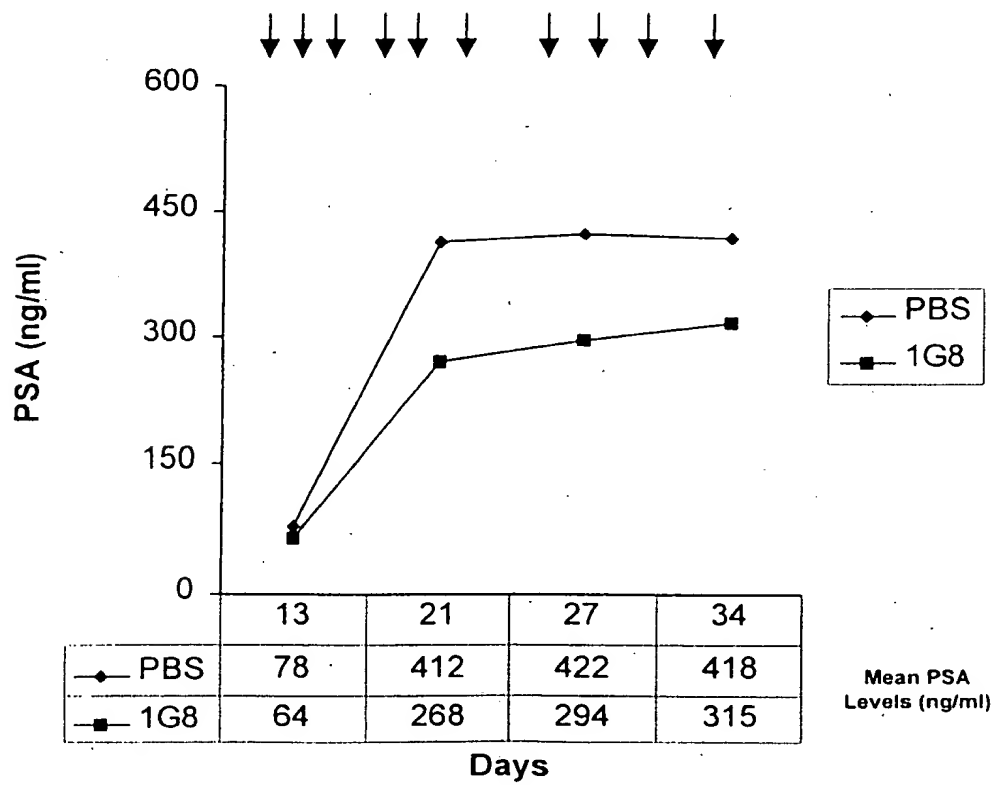
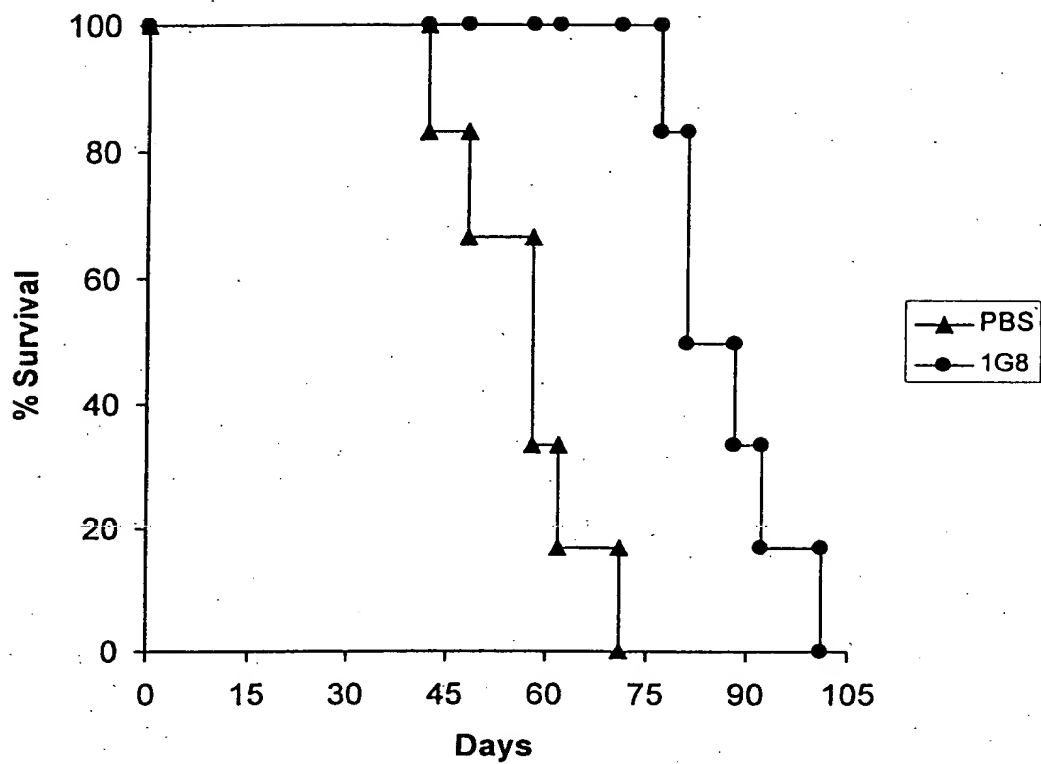


FIG. 67

A)



B)

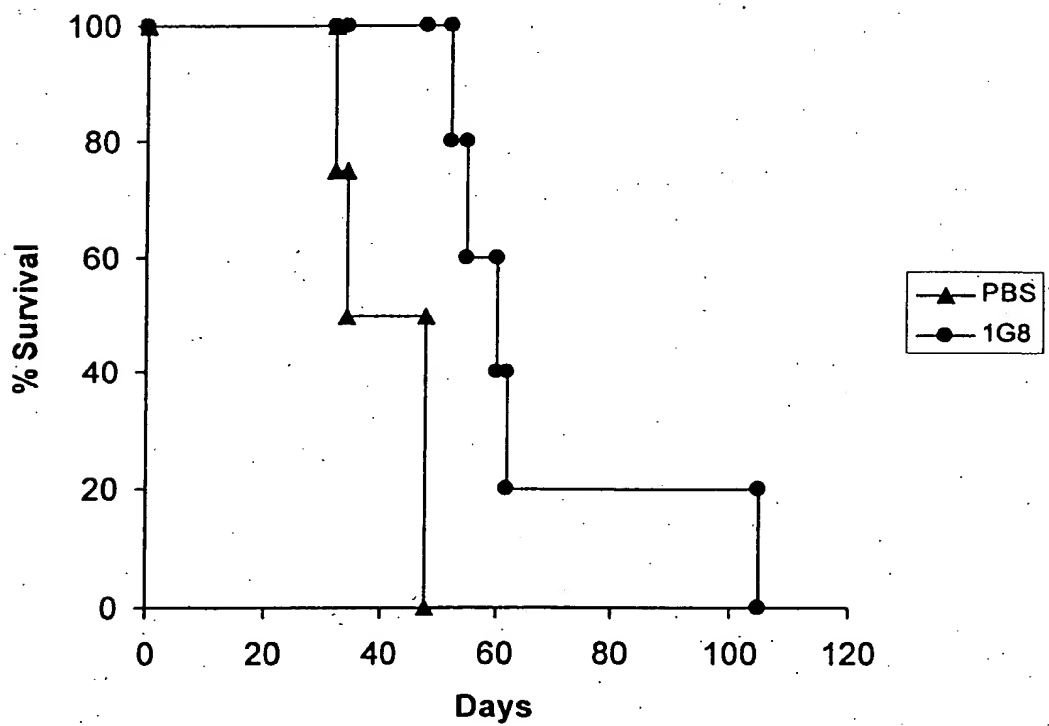
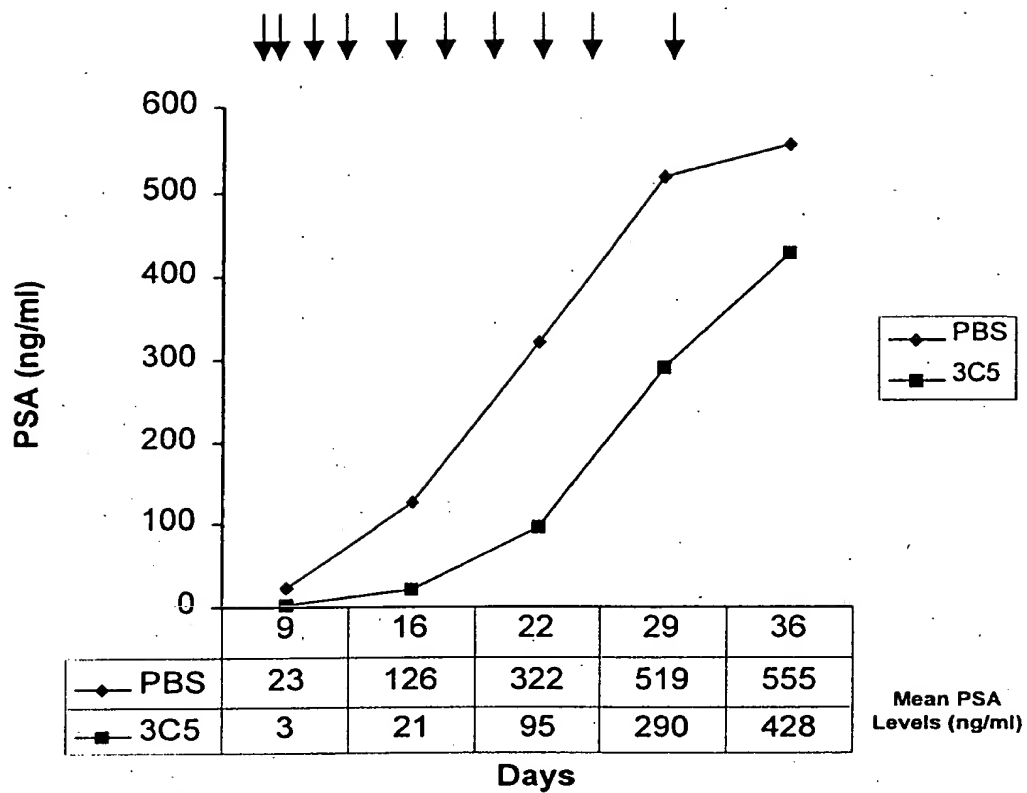


FIG. 68

A)



B)

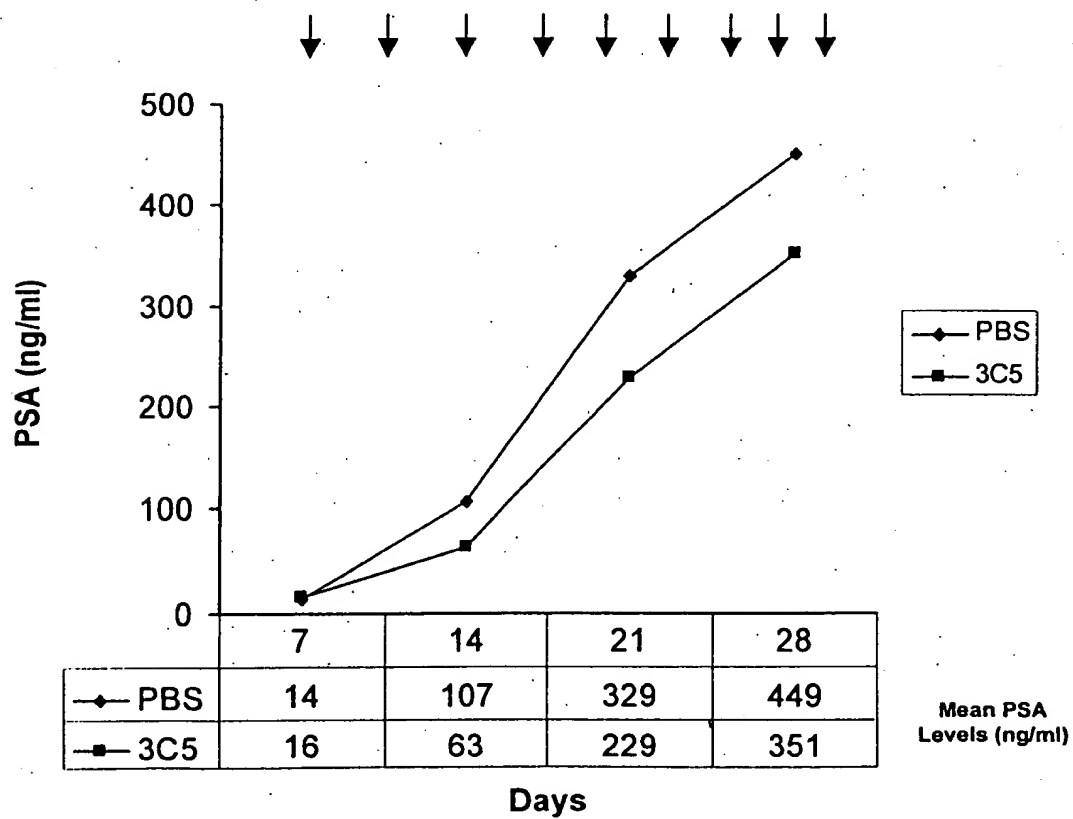
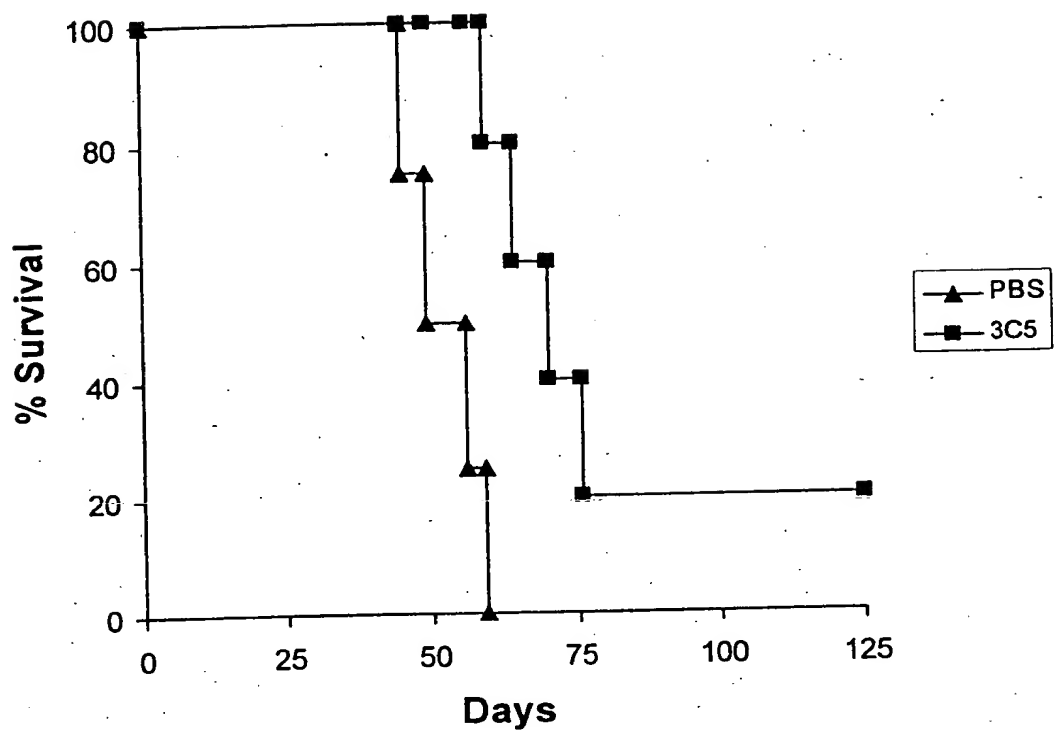


FIG. 69

A)



B)

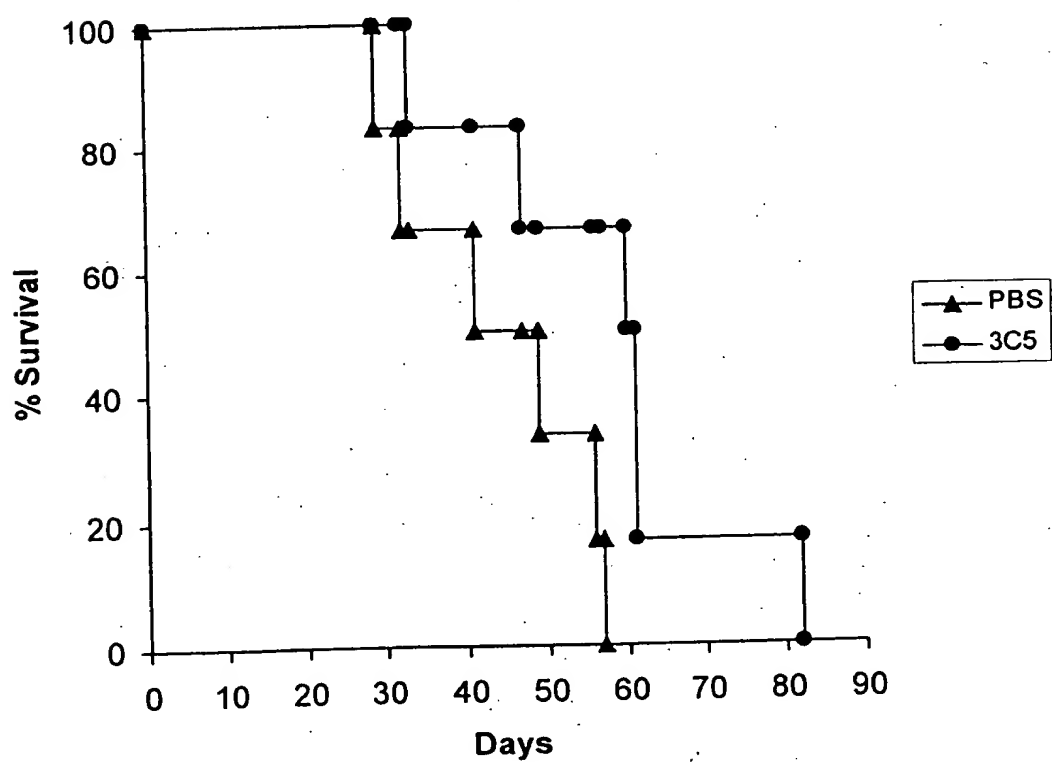
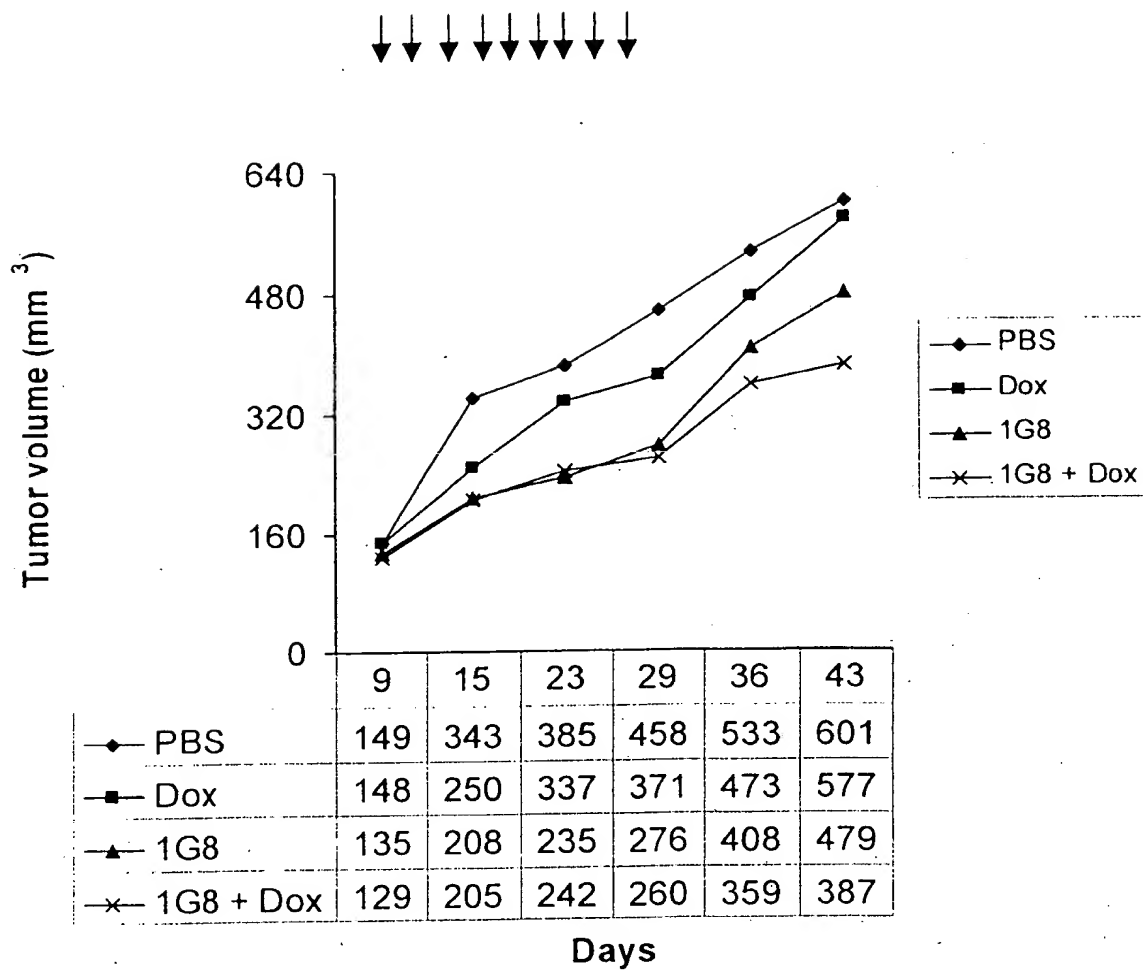


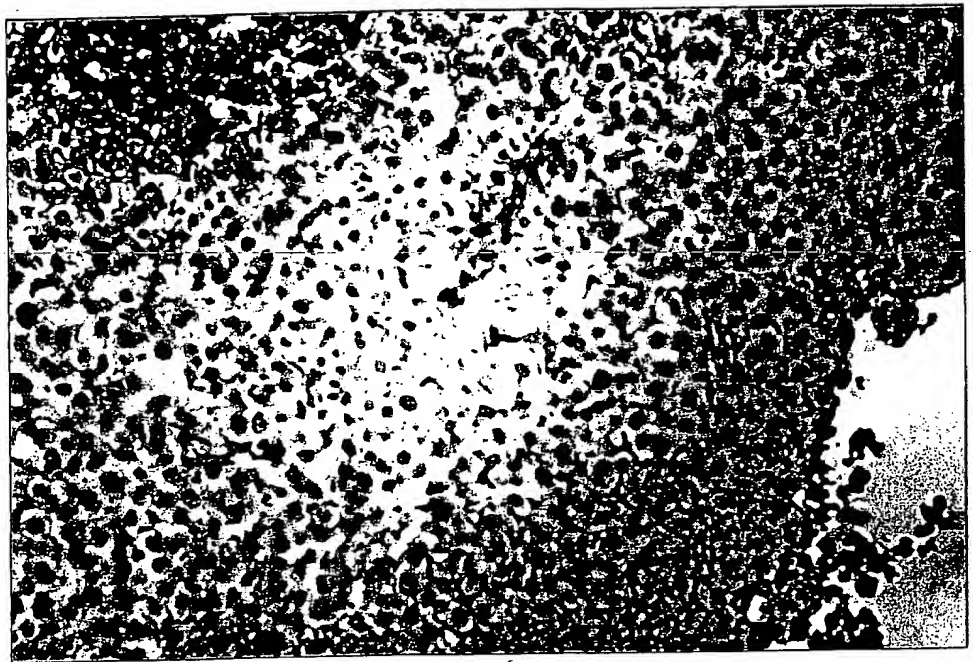
FIG. 70



09854811.072501
T05270.T1845860

FIG. 71

3C5 Treated



mIgG Treated

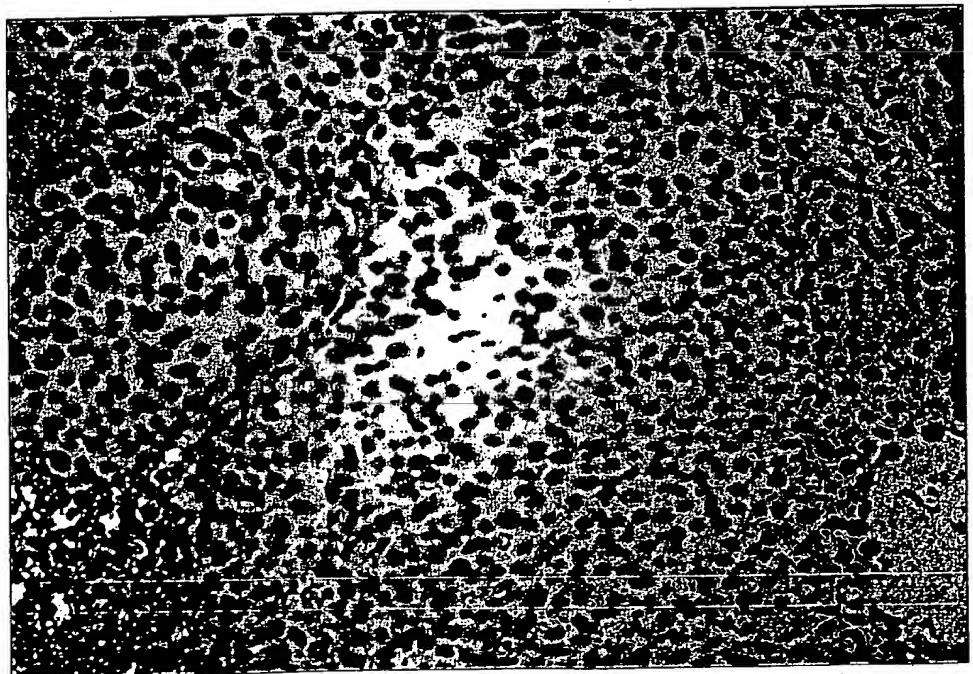


FIG. 72

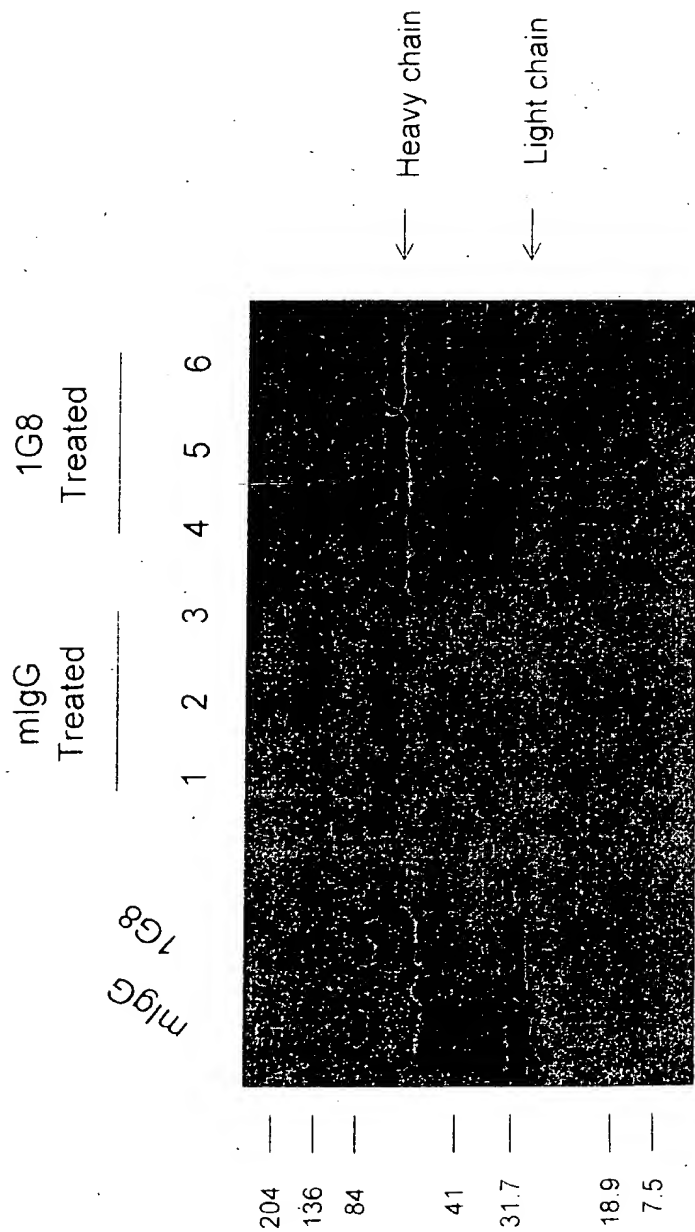


FIG. 73